OTN
ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Immune Globulin 50mg/ml, inj w/IV set	200 ml	49669-1614-01	900.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	50 ml	49669-1622-01	475.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	100 ml	49669-1623-01	950.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	200 ml	49669-1624-01	1,900.00	J1561	500mg	
Immune Globulin 100mg/ml, inj	10 ml	00026-0648-12	90.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	50 ml	00026-0648-20	450.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	100 ml	00026-0648-71	900.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	200 ml	00026-0648-24	1,800.00	J1561	500mg	800-998-9180
Immune Globulin, pwd	2.5 Gram	52769-0471-72	223.75	J1562	5Grams	
Immune Globulin, pwd	5 Gram	52769-0471-75	447.50	J1562	5Grams	
Immune Globulin, pwd	10 Gram	52769-0471-80	895.00	J1562	5Grams	
RHO (d) Immune Globulin, pwd	600 IU	60492-0021-01	142.00	J2792	100 IU	
RHO (d) Immune Globulin, pwd	1500 IU	60492-0023-01	324.50	J2792	100 IU	
RHO (d) Immune Globulin, pwd	5000 IU	60492-0024-01	1,081.50	J2792	100 IU	
Intron®-A						
Interferon Alpha 2B 3MIU/0.5ml	3 MIU PAK	00085-1184-02	36.34	J9214	1 MIU	800-521-7157
Interferon Alpha 2B 5MIU/0.5ml	5 MIU PAK	00085-1191-02	60.57	J9214	1 MIU	800-521-7157
Interferon Alpha 2B 10MIU/ML	10 MIU PAK	00085-1179-02	121.14	J9214	1 MIU	800-521-7157
Interferon Alpha 2B 6MIU/ml, inj	18 MIU MDV	00085-1168-01	218.04	J9214	1 MIU	800-521-7157
Interferon Alpha 2B 10MIU/ML, inj	25 MIU	00085-1133-01	302.87	J9214	1 MIU	800-521-7157
Interferon Alpha 2B, pwd	5 MIU	00085-0120-02	60.56	J9214	1 MIU	800-521-7157
Interferon Alpha 2B, pwd	10 MIU	00085-0571-02	121.14	J9214	1 MIU	800-521-7157
Interferon Alpha 2B, pwd	18 MIU	00085-1110-01	218.04	J9214	1 MIU	800-521-7157
Interferon Alpha 2B, pwd	25 MIU	00085-0285-02	302.87	J9214	1 MIU	800-521-7157
Interferon Alpha 2B, pwd	50 MIU	00085-0539-01	605.69	J9214	1 MIU	800-521-7157
Roferon® A						
Interferon Alpha 2A 3MIU/ML, inj	3 MIU	00004-2009-09	34.97	J9213	3 MIU	800-443-6676
Interferon Alpha 2A 6MIU/ml, inj	6 MIU	00004-2007-09	69.91	J9213	3 MIU	800-443-6676
Interferon Alpha 2A 9MIU/0.9ml, inj	9 MIU	00004-2010-09	98.44	J9213	3 MIU	800-443-6676
Interferon Alpha 2A 6MIU/ml, inj	18 MIU	00004-2011-09	209.60	J9213	3 MIU	800-443-6676
Interferon Alpha 2A 36MIU/ml, inj	36 MIU	00004-2012-09	419.26	J9213	3 MIU	800-443-6676
Camptosar®						
Irinotecan HCL 20mg/ml, inj	2 ml	00009-7529-02	248.03	J9206	20mg	800-242-7014
Irinotecan HCL 20mg/ml, inj	5 ml	00009-7529-01	620.09	J9206	20mg	800-242-7014
Leucovorin Calcium, pwd	50 mg	55390-0051-10	18.44	J0640	50mg	
Leucovorin Calcium, pwd	100 mg	55390-0052-10	35.00	J0640	50mg	
Leucovorin Calcium, pwd	200 mg	55390-0053-01	78.00	J0640	50mg	
Leucovorin Calcium, pwd	350 mg	58406-0623-07	137.94	J0640	50mg	800-321-4669
Lupron®						
Leuprolide Acetate, pwd	7.5 mg	00300-3642-01	623.79	J9217	7.5mg	800-453-8438
Leuprolide Acetate, pwd	22.5 mg	00300-3346-01	1,871.37	J9217	7.5mg	800-453-8438
Lorazepam 2mg/ml, inj	1 ml	00008-0581-04	9.85	J2060	2mg	
Lorazepam 2mg/ml, inj	10 ml	00008-0581-01	87.74	J2060	2mg	
Lorazepam 4mg/ml, inj	10 ml	00008-0570-01	109.66	J2060	2mg	
Lorazepam 2mg/ml, inj	1 ml syringe	00008-0581-02	10.39	J2060	2mg	
Mannitol 25%, inj	50 ml	00074-4031-01	6.13	J2150	50ml	
Mustargen®						
Mechlorethamine HCl, pwd	10 mg	00006-7753-31	11.59	J9230	10mg	800-994-2111
Megace®						
Megestrol Acetate 20mg Tablet	100 tabs	00015-0595-01	75.68			800-872-8718
Megestrol Acetate 40mg Tablet	100 tabs	00015-0596-41	134.96			800-872-8718
Megestrol Acetate 40mg Tablet	250 tabs	00015-0596-46	330.68			800-872-8718
Megestrol Acetate 40mg Tablet	500 mg tabs	00015-0596-45	647.88			800-872-8718
Megestrol Acetate oral susp 40mg/ml	240 ml	00015-0508-42	144.10			800-872-8718
Alkeran®						
Melphalan HCL, pwd	50 mg	00173-0130-93	382.61	J9245	50mg	800-722-9294
Melphalan 2mg Tablet	50 tabs	00173-0045-35	109.21	J8600	2mg	800-722-9294
Mesnex™						
Mesna 100mg/ml, inj	10 ml	00015-3563-02	192.16	J9209	200mg	800-872-8718
Methotrexate Sodium, pwd	20 mg	58406-0673-01	5.03	J9250	5mg	800-321-4669
Methotrexate Sodium, pwd	1 Gram	58406-0671-05	61.44	J9260	50mg	800-321-4669
Methotrexate Sodium 25mg/ml, inj	2 ml	55390-0031-10	6.88	J9260	50mg	
Methotrexate Sodium 25mg/ml, inj	4 ml	55390-0032-10	8.75	J9260	50mg	
Methotrexate Sodium 25mg/ml, inj	8 ml	55390-0033-10	17.50	J9260	50mg	
Methotrexate Sodium 25mg/ml, inj	10 ml	55390-0034-10	26.88	J9260	50mg	
Methotrexate Sodium 25mg/ml, inj	2 ml	58406-0681-14	4.75	J9260	50mg	800-321-4669
Methotrexate Sodium 25mg/ml, inj	10 ml	58406-0681-17	20.48	J9260	50mg	800-321-4669
Methotrexate Sodium 2.5mg Tablet	100 tabs	00555-0572-02	362.95	J8610	2.5mg	

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Methotrexate Sodium 2.5mg Tablet	36 tabs	00555-0572-35	130.05	J8610	2.5mg	
Mutamycin®						
Mitomycin, pwd	5 mg	00015-3001-20	134.11	J9280	5mg	800-872-8718
Mitomycin, pwd	20 mg	00015-3002-20	452.91	J9290	20mg	800-872-8718
Mitomycin, pwd	40 mg	00015-3059-20	915.09	J9291	40mg	800-872-8718
Novantrone®						
Mitoxantrone HCl 2mg/mL, inj	10 ml	58406-0640-03	939.04	J9293	5mg	800-321-4669
Mitoxantrone HCl 2mg/mL, inj	12.5 ml	58406-0640-05	1,173.76	J9293	5mg	800-321-4669
Mitoxantrone HCl 2mg/mL, inj	15 ml	58406-0640-07	1,408.55	J9293	5mg	800-321-4669
Sandostatin®						
Octreotide Acetate 50mcg/ml, inj	1 ml	00078-0180-03	6.07	J9999/J3490		800-257-3273
Octreotide Acetate 100mcg/ml, inj	1 ml	00078-0181-03	11.77	J9999/J3490		800-257-3273
Octreotide Acetate 500mcg/ml, inj	1 ml	00078-0182-03	56.80	J9999/J3490		800-257-3273
Sandostatin LAR® Depot						
Octreotide Acetate, pwd	10 mg	00078-0340-B4	1,368.75	J2352	1mg	800-257-3273
Octreotide Acetate, pwd	20 mg	00078-0341-B4	1,368.75	J2352	1mg	800-257-3273
Octreotide Acetate, pwd	30 mg	00078-0342-B4	2,053.12	J2352	1mg	800-257-3273
Zofran®						
Ondansetron HCL 2mg/ml, Inj	20 ml	00173-0442-00	256.40	J2405	1mg	800-745-2967
Ondansetron HCL 2mg/ml, Inj	2 ml	00173-0442-02	25.64	J2405	1mg	800-745-2967
Ondansetron 32mg/50ml, premixed bag	50 ml	00173-0461-00	206.41	J2405	1mg	800-745-2967
Neumega®						
Oprelvekin, pwd	5 mg	58394-0004-01	248.75	J2355	5mg	888-638-6342
Taxol®						
Paclitaxel 6mg/ml, inj	30 mg	00015-3475-30	182.63	J9265	30mg	800-872-8718
Paclitaxel 6mg/ml, inj	100 mg	00015-3476-30	608.76	J9265	30mg	800-872-8718
Paclitaxel 6mg/ml, inj	300 mg	00015-3479-11	1,826.25	J9265	30mg	800-872-8718
Aredia®						
Pamidronate disodium pwd	30 mg	00083-2601-04	244.25	J2430	30mg	800-257-3273
Pamidronate disodium pwd	90 mg	00083-2609-01	678.31	J2430	30mg	800-257-3273
Nipent®						
Pentostatin pwd	10 mg	62701-0800-01	1,645.00	J9268	10mg	800-340-8667
Prochlorperazine 5mg/ml, Inj	10 ml	00007-3343-01	41.08	J0780	Up to 10mg	800-699-3806
Prochlorperazine 10mg tab	100 tabs	00007-3367-20	94.50	Q0165	10mg	800-699-3806
Zantac®						
Ranitidine 25mg/ml, inj	2 ml	00173-0362-38	3.98	J2780	25mg	
Respigam®						
Respiratory Syncytial Virus Immune globul	20 ml	60574-2102-01	450.50	J1565	50mg	
Respiratory Syncytial Virus Immune globul	50 ml	60574-2101-01	755.15	J1565	50mg	
Rituxan®						
Rituximab 10mg/ml, inj	10 ml	50242-0051-21	442.41	J9310	100mg	800-530-3083
Rituximab 10mg/ml, inj	50 ml	50242-0053-06	2,212.08	J9310	100mg	800-530-3083
Zanosar®						
Streptozocin, pwd	1 Gram	00009-0844-01	114.69	J9320	1Gram	800-242-7014
Vumon®						
Teniposide 10mg/ml, inj	5 ml	00015-3075-19	205.60	J9999	50mg	800-872-8718
Thioplex®						
Thiotepa, pwd	15 mg	58406-0661-02	105.58	J9340	15mg	800-321-4669
Hycamtin®						
Topotecan, pwd	4 mg	00007-4201-01	603.95	J9350	4mg	800-699-3806
Topotecan, pwd	4 mg	00007-4201-05	603.95	J9350	4mg	800-699-3806
Herceptin®						
Trastuzumab, pwd	440 mg	50242-0134-60	2,262.58	J9355	10mg	800-530-3083
Neutrexin®						
Trimetrexate, pwd	25 mg, 10's	58178-0020-10	735.00	J3305	25mg	800-887-2467
Trimetrexate, pwd	25 mg, 50's	58178-0020-50	3,675.00	J3305	25mg	800-887-2467
Trimetrexate, pwd	200 mg	58178-0021-01	588.05	J3305	25mg	800-887-2467
Urokinase, pwd	5000 IU	00074-6111-01	59.55	J3364	5000IU	
Urokinase, pwd	9000 IU	00074-6145-02	103.91	J3364	5000IU	
Vinblastine sulfate pwd	10 mg	55390-0091-10	21.25	J9360	1mg	
Vinblastine sulfate 1mg/ml, inj	10 ml	63323-0278-10	43.23	J9360	1mg	
Vincristine sulfate 1mg/ml, inj	1 ml	00013-7456-86	43.23	J9370	1mg	800-242-7014
Vincristine sulfate 1mg/ml, inj	1 ml	61703-0309-06	31.25	J9370	1mg	
Vincristine sulfate 1mg/ml, inj	2 ml	00013-7466-86	86.46	J9375	2mg	800-242-7014
Vincristine sulfate 1mg/ml, inj	2 ml	61703-0309-16	38.25	J9375	2mg	
Navelbine®						
Vinorelbine 10mg/ml, inj	1 ml	00173-0656-01	79.48	J9390	10mg	800-423-6869
Vinorelbine 10mg/ml, inj	5 ml	00173-0656-44	397.38	J9390	10mg	800-423-6869

10A

BP 01295

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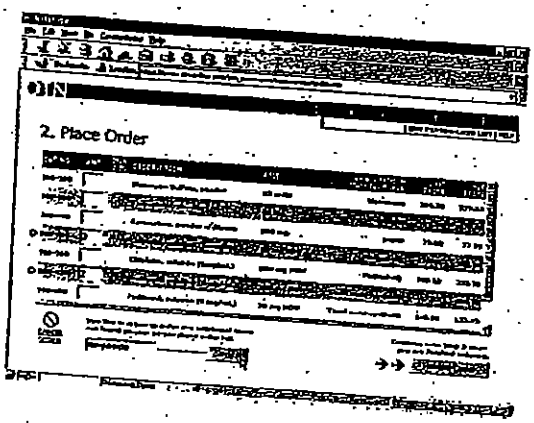
Management Reports Online

Access Your Practice's Monthly Inventory Management Reports Online!

OTN is committed to continually improving your access to data and to addressing your concerns regarding your practice's profitably. To that end, we are happy to announce that as OTN customers, you are now able to access your monthly inventory management reports via OTN-Online.



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- ✓ Access your current monthly purchase history, which is updated daily to reflect your previous day's totals.
- ✓ Track purchase history for multiple sites.
- ✓ Compare the current month's quantity and cost, by item, to the previous three-month averages.

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Comments and suggestions are welcome. Address them to: Peggy Lehmann, Editor, The Network News, Oncology Therapeutics Network, 395 Oyster Point Blvd., Suite 405, So. San Francisco, CA 94080.

BP 01296

October 2000

OTN THE NETWORK NEWS

ONCOLOGY THERAPEUTICS NETWORK

AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS

Route To:
- ☐ Physician
- ☐ Office Manager
- ☐ Oncology Nurse
- ☐ Pharmacist
- ☐ Business Office
- ☐ _____

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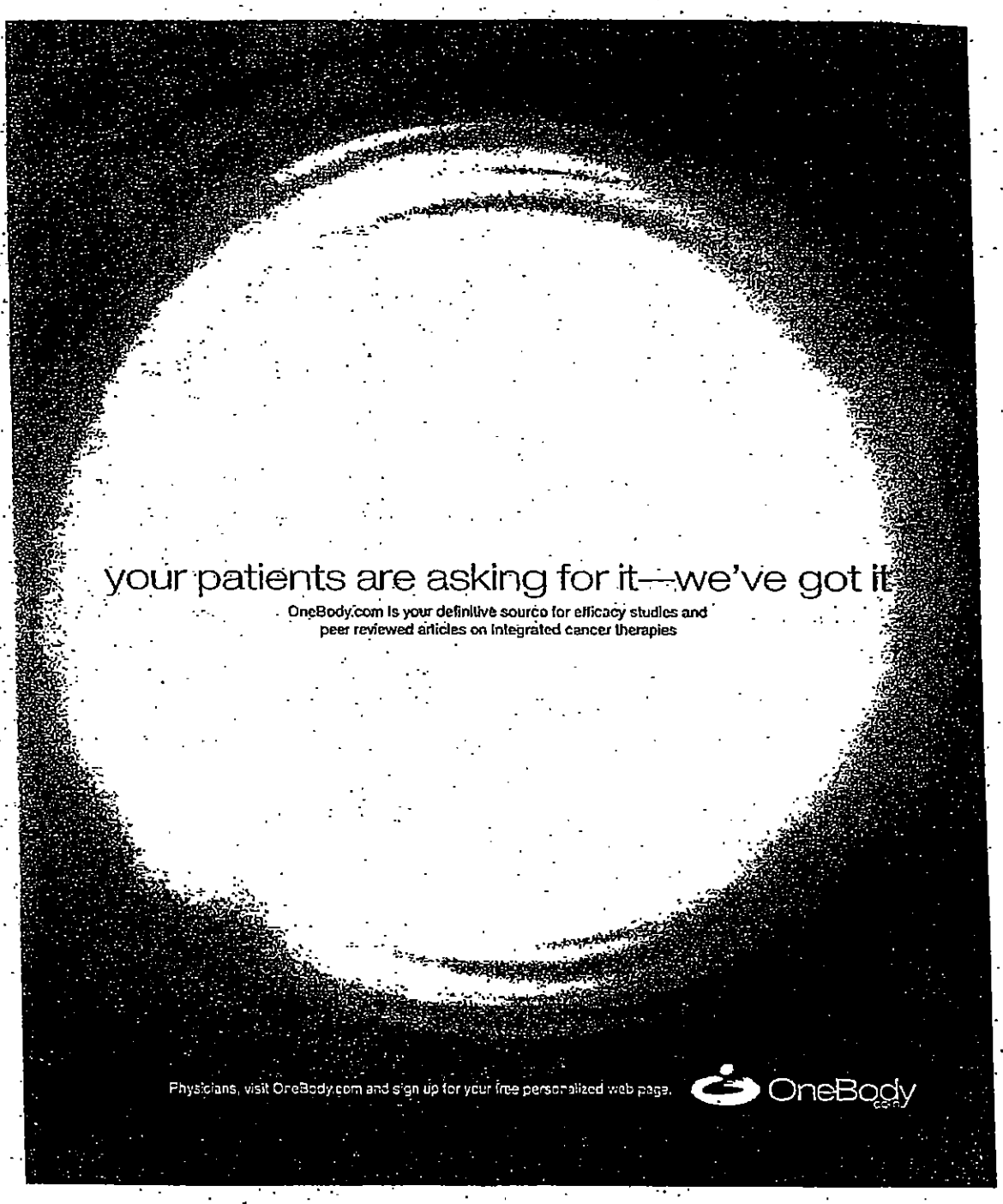

REIMBURSEMENT ASSISTANCE

Bobbi Buell, MBA
President, Documedics

ONCOLOGY THERAPEUTICS NETWORK

New ICD-9-CM Codes—Anemia in the Red?

Yes, it's that time of year when the new ICD-9-CM codes are introduced to the U.S. These codes can be used after October 1, 2000 and not before then. Payers adopt these at different times, so check with any insurance carrier before billing this year.

BIG NEWS! Anemia codes change: What this will mean for PROCRIT® billing we don't know. However, do not use these codes until you confirm that your carrier has changed your guidelines. Our old code, 285.9, has not been deleted. So, you can use it without fear until guidelines are changed. The new codes are: 285.21, anemia in end-stage renal disease; 285.22, anemia in neoplastic disease (says nothing about chemo here) and, 285.29, anemia in chronic disease. Again, these are informational until October 1, 2000 and, after that, check your Carrier Bulletin or call PROCRITline at (800) 553-3851.

Infectious Disease: 007.5, Cyclosporiasis; 082.40, Unspecified ehrlichiosis; 082.41, Ehrlichiosis chaffensis; and, 082.49, other ehrlichiosis.

Mental Illnesses: 294.10, Dementia in conditions classified elsewhere without behavioral disturbance; and, 294.11, Dementia in conditions classified elsewhere with behavioral disturbance.

Eyes: 372.81, Conjunctivochalasis and 372.89, Other disorders of the conjunctiva.

Respiratory: 477.1, Allergic rhinitis, due to food. New asthma codes include 493.02, Extrinsic asthma with acute exacerbation; 493.12, Intrinsic asthma with acute exacerbation; and 22, Chronic obstructive asthma with acute exacerbation. Plus, there is 494.0, Bronchiectasis without acute exacerbation and 494.1, Bronchiectasis with acute exacerbation.

Abdominal: 558.3, Allergic gastroenteritis and colitis.

Prostate: Code 600 used to be benign prostatic hypertrophy—easy to code. Now we have 600.0, Benign hypertrophy of the prostate; 600.1, Nodular prostate; 600.2; Cyst of the prostate, 600.3; and, 600.9 unspecified hyperplasia of the prostate.

Pregnancy: For prolonged pregnancy, see 645.10, Post term pregnancy, unspecified as to episode of care or not applicable; 645.11, Post term pregnancy, delivered, with or without mention of antepartum condition; 645.12, Post term pregnancy, antepartum condition or complication; 645.20, Prolonged pregnancy, delivered, with or without mention of antepartum condition; and, 645.22, Prolonged pregnancy, antepartum condition or complication.

Skin: 692.75, Disseminated superficial actinic porokeratosis (DSAP). There are new codes for ulcers of the skin: 707.1x with "x" being the location on the lower limb.

Musculoskeletal: 727.83, Plica syndrome.

Symptoms: 781.91, Loss of height; 781.92, Abnormal posture; 783.21, Loss of weight (can be on most cancer claims); and, 783.22, Underweight. If a patient looks emaciated, you can use 783.40, Unspecified lack of normal physiological development; and, 783.41, Failure to thrive. For procrastinators, we have 783.42, Delayed milestones. For little patients, there are 783.43, Short stature or 783.7, Adult failure to thrive. 790.01 is for a precipitous drop in the hematocrit and 790.09 is for other abnormality of the red blood cells. 792.5 is for cloudy dialysis effluent. 790.09 is for other adverse food reactions, not elsewhere classified.

Complications: 996.87, complications of transplanted organ, intestine.

V-codes: For allergies, we have V15.0x with x being 1 for peanuts; 2 for milk products; 3 being eggs; 4 being seafood; and, 5 for other foods. We jump from food allergies to other fifth digits for V15.0x: 6 is insects; 7 is latex; 8 is radiographic dye; and, 9 is other allergy, other than medicinal agents. V21.3x is for low birth weight where x is the weight in grams. V26.21 is used for fertility testing, while V26.22 is for aftercare following sterilization reversal. V26.29 is used for other investigation and testing. V42.84 is for organ or tissue replaced by transplant, intestines. V45.7x is Acquired absence of an organ where fifth digits starting with 4 through 9 are organs that are missing.

More V-codes: V49.81 is Post-menopausal status (age-related) (natural). V49.89 is a vague one—other specified conditions influencing health status. V56.3x where x is 1 or 2 is adequacy testing for hemo- or peritoneal dialysis. You might want to use this one—Encounter for therapeutic drug monitoring, V56.83. V67.0x is for follow up after surgery where x is exams done after surgery. V71.81, observation for suspected abuse and neglect.. V71.89, Observation for other specified, suspected conditions.

And, yet more V-codes for screening cancer: There are new V76.x codes for special screening for specific neoplasms, i.e. cancer. They are V76.46-V76.81. Neoplasms involved are ovary, vagina, intestine, colon, small intestine, nervous system, and others. Special screening can mean genetic testing or anything that is not part of the 'normal' screening tests for a type of cancer. V77.91 is screening for lipoid disorders. V77.99, Other and unspecified nutritional, metabolic, and immunity disorders. V82.81, Special screening for osteoporosis and V82.89, Special screening for other specified conditions.

Revised codes: 564.1, Irritable bowel syndrome. V26.3, Genetic counseling and testing. V76.49, Special screening for malignant other sites.

There are many deleted codes. Check your new ICD-9-CM book or the HCFA website at www.HCFA.gov.

ONCOLOGY THERAPEUTICS NETWORK

Is your practice receiving the best pricing possible?

Tips for Negotiating Your Manufacturer Contracts

Karen Weiss, Customer Analysis Specialist

Marilyn Ping, Manager, Customer Analysis

We at OTN appreciate the unique financial pressures that concern the office-based oncology marketplace. While we strive to provide exceptional service, we also welcome any opportunity to add further value to our distribution relationship. In this regard, OTN is proud to honor any manufacturer-negotiated contract designating OTN as the prime vendor. These contracts allow your practice to buy key products at substantial cost savings.

How does it work?

- Contracts are awarded to individual practices or group accounts, typically for a term of one year. Most manufacturer contracts are based on purchase volume, and are re-negotiated periodically due to performance changes.
- Manufacturers recognize practices under contract using either a Federal Drug Enforcement Agency (DEA) license unique to a physician at the practice, or a Health Industry Number (HIN) unique to each practice location. An HIN is a number given to every healthcare organization from HIBCC to monitor interactions between facilities. OTN has developed a relationship with HIBCC allowing for receipt of HIN's directly without inconvenience to the practice. Similarly, most manufacturers can access HIN information for your practice's location.
- Whether your site is part of a multi-site practice or group affiliation, every facility in your organization needs to be uniquely attached to a manufacturer contract either with a DEA for a physician practicing at that facility or with a HIN. If you add a satellite site to your practice or have changes in your group membership, you must contact your manufacturer representative (see list below) to add that site to existing contracts.

In negotiating a new contract, information about all facilities in an organization should be provided to the manufacturer to insure that every location receives the same contract pricing. OTN can not implement contract pricing for any given site without receiving a contract that directly identifies the site in an organization.

- Most manufacturers will ask you to provide the name of a prime vendor. By including OTN as a prime vendor, you ensure that we will receive notification of contract updates, renewals, and additions in a timely fashion. This process helps OTN extend the best price to you as efficiently as possible.
- At OTN, we have a dedicated team of contract specialists in our Customer Analysis and Pricing Department. We are committed to implementing a customer contract within two business days after receipt. Furthermore, we have developed the most sophisticated contract delivery system in the industry, to ensure timely notification of contract changes. When our manufacturing partners provide a one-week notice of new contracts, or changes to existing contracts, OTN can ensure a smooth, hassle-free process up-front.
- Through the efforts of our Business Development Department, we have negotiated relationships with most manufacturers allowing us to honor your contract price without an added fee. OTN reserves the right to add an administrative fee to contracts if the manufacturer does not offer OTN an administrative fee.
- Now available! You can view existing contracts using our website OTN Online at www.otn-online.com. In the account profile section of the web site, contracts can be viewed for all affiliated facilities. Please take the time to review this section for any contracts not currently listed.

If you have not yet designated OTN as a prime vendor for your practice, please contact the appropriate party listed. Don't forget to make sure that each manufacturer has a complete list of your site's) Federal DEA or HIN information. OTN looks forward to fully serving our customers with the best customer service at a competitive price.

Manufacturer contact list:

Amgen	Contact Elizabeth Hazelton at (800) 926-4369, ext. 74493
Glaxo:	(800) 445-2964 or contact your local representative
Immunex:	Contact Lisa Addicott at (800) 466-8639
SKB:	(800) 366-8900 or contact your local representative
Aventis (HMR)	(800) 362-7466 or contact your local representative
Other	Contact your local representative

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Schering®

INTRON® A

Interferon Alfa-2b, Recombinant
for Injection

Multidose Pen

NOW AVAILABLE IN A UNIQUE DELIVERY SYSTEM

INTRON® A Multidose Pen		Total Dose and Volume	Indications
	3 MIU	18 MIU (6 doses x 3 MIU/0.2 mL)*	Chronic hepatitis C
	5 MIU	30 MIU (6 doses x 5 MIU/0.2 mL)*	Chronic hepatitis B, follicular lymphoma
	10 MIU	60 MIU (6 doses x 10 MIU/0.2 mL)*	Chronic hepatitis B, malignant melanoma

[illegible] should be stored between 2° and 8°C (36° and 46°F). INTRON® A is stable for up to 2 days at 30°C (86°F).

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Breast Cancer Prevention: Current Strategies

Alison Shore, MS

Introduction

Breast cancer is the most commonly diagnosed disease in Western women and will result in 41,000 to 45,000 deaths in 2000.[1] Because current data indicate that incidence of the disease can be reduced, a focus on breast cancer prevention is warranted and wise. Choosing a preventive method depends on several factors, the most significant of which is the patient's risk of developing breast cancer. Also important are consideration of the method's potential benefits compared with its risks and patient comfort with the chosen method. Because estrogen production plays an important role in a woman's likelihood of developing cancer, recent research efforts have focused on the activity of selective estrogen-receptor modulators (SERMs), including tamoxifen and raloxifene. Other preventive methods include prophylactic mastectomy, a highly successful but still-controversial practice, and lifestyle modifications. This article discusses current preventive strategies and notes their advantages, disadvantages, and relevance related to a woman's risk level.

Table 1. Gail Model Criteria for Determining Breast Cancer Risk

- Age at first live birth (or nulliparity)
- Age at menarche
- Atypical hyperplasia
- Current age
- Number of breast biopsies
- Number of first-degree relatives with breast cancer (i.e., mother, sisters, daughters)
- Race

Risk Assessment

Determining a woman's risk of developing breast cancer relies mainly on individual assessment of the gynecologic and endocrinologic events that have shaped her life. In particular, most clinicians agree that the level of circulating estrogen to which a woman has been exposed is key. For instance, if a woman experiences early-age menarche (ie, 11–14 years of age) and late-age menopause (ie, 55 years of age), she is exposed to more circulating estrogen because she has had more lifetime menstrual cycles; she has a 30% to 50% higher risk of developing breast cancer than does a woman experiencing menarche at age 16 and menopause between the ages of 45 and 55. A woman who stops menstruating at 45 years of age or younger, however, has a 30% lower risk of developing the disease. Likewise, a woman who gives birth before the age of 20 has a marked reduction in the likelihood of developing breast cancer; the reasons for this are complex, but fertilization and pregnancy keep progesterone levels elevated, which ultimately causes breast cell differentiation and reduces proliferation.[2] Conversely, progesterone stimulates cell proliferation following ovulation and, if pregnancy does not occur, progesterone levels fall, breast cell division decreases, and apoptosis follows.

These factors and others are included in a model of risk assessment developed by Gail and colleagues at the National Cancer Institute (NCI). "High risk" is defined as risk of breast cancer equal to or greater than that of a 60-year-old woman (advanced age is the leading risk factor for breast cancer). In addition to the previously discussed estrogen-related factors, a woman's current age, personal and family history, and race are important criteria in evaluating her risk of breast cancer (Table 1).[3] The model uses a multivariate logistic regression method in which combinations of risk factors are used to estimate the probability of breast cancer occurrence over time.

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Tamoxifen

Since its Food and Drug Administration (FDA) approval in 1978, tamoxifen has been the leading hormonal treatment of postmenopausal women with metastatic breast cancer. It is now also used as adjuvant therapy of early breast cancer, with substantial data confirming its efficacy in increasing disease-free and overall survival rates.

Encouraging clinical data from two adjuvant tamoxifen trials—one by the National Surgical Adjuvant Breast and Bowel Project (NSABP) and the other by the Early Breast Cancer Trialists Collaborative Group—were the impetus for further study of tamoxifen as prophylactic therapy in the NSABP's Breast Cancer Prevention Trial (BCPT).[2] The BCPT randomized 13,388 high-risk women to receive either tamoxifen 20 mg/d or placebo for 5 years. Tamoxifen reduced the risk of both invasive breast cancer by 49% ($P < .00001$) and noninvasive breast cancer by 50% ($P < .002$), statistics so compelling that the trial was ended 14 months before the planned completion.[1] Tamoxifen also reduced hip, radial, and spine fractures. The benefits of this SERM appear to be limited to estrogen-receptor (ER)–positive tumors, which account for 75% of all breast cancers; whether tamoxifen has any cytotoxic activity in ER-negative tumors remains uncertain.[1]

Tamoxifen is not without its detractors, who continue to be wary of administering a medication that has been shown to cause serious side effects, such as a more than 2-fold increased risk of endometrial cancer and a 3-fold heightened risk of pulmonary embolism in women older than 50.[1,4] Moreover, results of two other trials (Royal Marsden Trial and Italian Tamoxifen Prevention Study) did not corroborate the findings of the BCPT, reporting no significant preventive properties of tamoxifen; however, eligibility criteria differed in these studies, and the Italian study was terminated early because of poor compliance.[2]

Despite concerns regarding tamoxifen's safety, indications for the agent grew in 1998, when it became the first agent to be approved by the FDA for cancer prevention—in this case, breast cancer in patients at high risk according to the Gail model.[1] Although not specifically mentioned in the FDA recommendations, the high-risk category should probably include patients with either lobular carcinoma in situ or ductal carcinoma in situ, or carriers of mutations in either the BRCA1 or BRCA2 genes.[1,2] In addition to determining a patient's risk status, the physician, along with the patient, must carefully consider the benefits and adverse effects of tamoxifen chemoprevention.

Raloxifene

As a SERM, raloxifene has estrogen agonist activity on lipid metabolism and preserves bone density, and has received FDA approval for both the prevention and treatment of osteoporosis.[1] In the Multiple Outcomes of Raloxifene Evaluation (MORE) trial of 7,705 postmenopausal women, raloxifene was evaluated for its ability to prevent bone fractures, but it also displayed activity in reducing the incidence of invasive breast cancer. At a median follow-up of 40 months, 13 women receiving raloxifene developed the disease, whereas 27 women receiving placebo developed breast cancer (relative risk, 0.24; CI, 0.13-0.44). Two other trial results showed that use of raloxifene, unlike tamoxifen, appears to cause no endometrial hyperplasia or cancer.[1]

Because the MORE trial focused on raloxifene's efficacy in osteoporosis, the drug's benefits in breast cancer must be further studied; the NCI is currently comparing tamoxifen and raloxifene in a head-to-head, randomized trial, the largest breast cancer prevention trial conducted to date.[1,2]

Prophylactic Mastectomy

Although surgical removal of a breast remains a viable option in breast cancer prevention, undergoing the radical procedure does not guarantee complete removal of potentially cancerous tissue. Furthermore, patients must often deal with the scars—both physical and emotional—of such highly invasive surgery.

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Nonetheless, results of a Mayo Clinic retrospective study of moderate- to high-risk patients who underwent prophylactic bilateral mastectomy revealed a 90% reduction in the incidence of breast cancer.[25] This procedure should be reserved for patients who have characteristics such as a strong personal or family history of breast cancer or in whom multiple breast biopsies have been performed.

Lifestyle Modifications

Women with a low to normal risk of breast cancer are not candidates for the more aggressive preventive techniques discussed previously. Instead, careful monitoring of lifestyle, which includes rigorous breast health surveillance (eg, annual mammography after the age of 40), is highly recommended. None of the following factors have been shown to prevent or reduce a woman's risk of developing breast cancer; however, adherence to these lifestyle recommendations contributes to overall good health and strengthens the likelihood of warding off many cancer types, including breast cancer.[2]

Weight Control

Most clinicians would probably agree that maintaining a healthy weight may reduce the risk of breast cancer development, although no studies have confirmed this belief. First, obesity may provide an opportunity for the proliferation of cancer cells because fat is a significant source of hormone substrates in postmenopausal women.[2] Second, results of a meta-analysis of case-control studies and several international comparisons have revealed that consumption of high-fat diets and other specific types of dietary fats might be linked to the development of breast cancer. These results were not, however, borne out in cohort studies, most notably in a 14-year study of 88,795 women whose daily fat consumption was either less than or equal to 20% or between 30% and 35% of total caloric intake; the women eating a higher-fat diet did not display a significantly increased relative risk of developing breast cancer.[2] Nonetheless, the American Cancer Society advocates a low-fat diet.

Smoking Cessation

Again, no studies have definitively proved that cigarette smoking induces breast cancer, but ample evidence shows that it increases the risk of lung cancer and heart disease. Because smoking offers no known health benefits, eliminating the use of tobacco can only contribute positively to a woman's health.

Limited Alcohol Consumption

Study data show that moderate to high intake of alcoholic beverages has been associated with increased breast cancer incidence.[2] An Italian case-control study, for example, compared breast cancer development in drinkers and nondrinkers; the age-adjusted odds ratio was 1.31 (confidence interval [CI], 1.13—1.53), with a significant association between risk and level of daily alcohol consumption ($P < .0005$).[6] Conversely, the Framingham study,[7] which was designed to study heart disease but also included a subanalysis of breast cancer, reported an inverse correlation between alcohol consumption and breast cancer. Nonetheless, serum estrogen levels have been shown to be higher in heavier drinkers,[8] and it has been postulated that alcohol stimulates increased estrogen production. Additionally, alcohol may induce negative effects by interfering with DNA repair, carrying carcinogens into breast tissue, or increasing exposure to toxic oxidants.[2]

Exercise

In the largest prospective study to date, Thune et al[9] evaluated the effects of exercise on the risk of breast cancer development. Results indicated that lean women who exercised at least 4 hours a week had the lowest cancer risk (relative risk, 0.28; CI, 0.11—0.70). Another study with a follow-up of 16 years also linked increased physical activity with a lowered risk of breast cancer ($P = .004$).[10]

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Hormone Use

Results of a prospective study of 37,105 women showed that use of hormone replacement therapy (HRT) for more than 5 years significantly increased the risk of breast cancer (relative risk, 2.65).[2] HRT's benefits, however, are well documented: relief of menopausal symptoms and improved bone density and cardiovascular function. Because 50% of women will die of cardiovascular-related disease, and breast cancer accounts for less than 4% of female deaths, the benefits of HRT may outweigh the potential risks.[1]

Less is known about oral contraceptive use, although a recent meta-analysis reported that current users had an increased relative risk of breast cancer (1.24; $P < .00001$) compared with women who had never taken oral contraceptives.[2] The effects of exogenous estrogen use require further clarification.

Conclusions and Future Directions

Women at high risk of developing breast cancer have several preventive options. Prophylactic mastectomy, despite the rigors of invasive surgery and its psychological aftermath, is recommended for women whose family history or personal medical history classifies them as likely candidates for breast cancer development; additionally, surgical intervention remains the most effective preventive method available. The FDA has approved the use of the SERM tamoxifen as chemotherapeutic prevention in women considered at high risk according to the Gail model. Tamoxifen has displayed notable activity in reducing the incidence of both invasive and noninvasive breast cancer, but it also produces deleterious effects, such as an increase in endometrial cancer and thromboembolic events in women older than 50 years. Another SERM, raloxifene, already approved for use in preventing and treating osteoporosis, also appears to be a promising agent in the prevention of breast cancer. It is currently being compared with tamoxifen to determine which agent is superior in providing efficacy with limited side effects. Finally, a woman whose lifestyle incorporates moderation in diet and alcohol consumption, moderate exercise, and no tobacco use will reap overall health benefits, which may in turn diminish her likelihood of developing cancer.

Other chemoprevention strategies, including the use of luteinizing hormone-releasing hormone (LHRH) agonists and retinoids, are in early stages of development. LHRH antagonists reduce breast cell proliferation and retinoids have antitumor effects in mammary tissues, among other tumor types. Large-scale studies are needed to define the role of these agents in breast cancer prevention.

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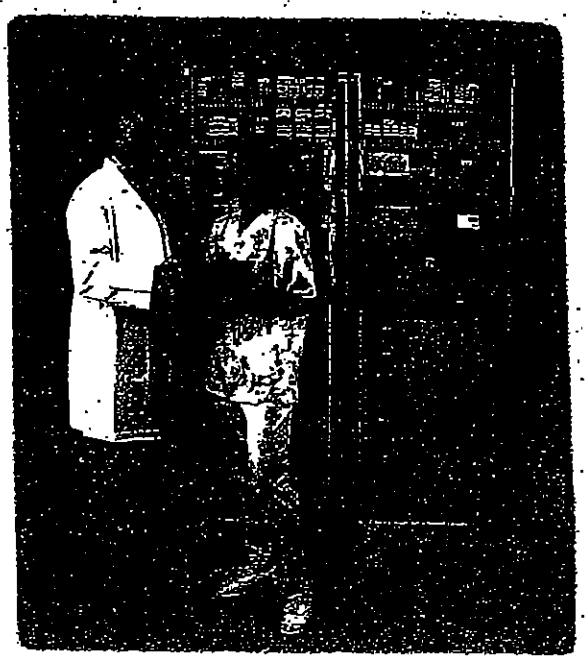

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Oral Fluorinated Pyrimidines for Treatment of Metastatic Breast and Colorectal Cancer

Imad Treish, PharmD

Introduction

Patient quality of life and comfort and cost of chemotherapy have become increasing concerns for oncologists over the past decade. With advances in ambulatory infusion technology and more easily administered chemotherapy regimens, many cancer patients are able to receive chemotherapy in the outpatient setting or at home, simplifying the treatment process.[1,2] Oral chemotherapy and supportive care drugs are generally less expensive and easy to administer than are their intravenous (IV) counterparts. Although oral administration of many chemotherapy agents is feasible, the erratic absorption and unpredictable pharmacokinetic profiles of these agents have limited their widespread use.

The development of oral fluoropyrimidine (OFP) analogues has renewed the interest in orally administered chemotherapy drugs. A number of OFPs have been developed, including capecitabine (Xeloda®, Hoffman La Roche), uracil-tegafur-leucovorin (UFT-LV) (Orzel™, Bristol-Myers Squibb), eniluracil (Glaxo Wellcome), and S1. In addition to ease of administration and predictable pharmacokinetics, OFPs appear to lack the toxicity associated with IV bolus administration of the fluoropyrimidine fluorouracil (5-FU). Furthermore, OFPs may circumvent some of the resistance mechanisms that lead to failure of IV 5-FU. Because continuous-infusion (CI) 5-FU proved superior to bolus administration (ie, improved response rates [RRs], improved overall survival times, reduced hematologic toxicities),[3] the ability of the new OFPs to maintain consistent 5-FU plasma concentrations, thus mimicking CI 5-FU, is another advantage of these new agents.

This article reviews the clinical pharmacology of the new OFPs and discusses results of clinical trials with capecitabine, UFT-LV, and eniluracil. Other agents are still in early stages of clinical development.

Pharmacology of 5-FU and OFPs

5-FU

5-FU is a prodrug that requires sequential phosphorylation to 5-fluorodeoxyuridine (5-FdUMP), 5-fluorodeoxyuridine triphosphate (5-FdUTP), and fluorouridine triphosphate (5-FUTP) for activation. Three mechanisms of cytotoxicity have been proposed for 5-FU.[4] The primary mechanism of 5-FU cytotoxicity in human tumors is the irreversible inhibition of thymidylate synthetase (TS) by FdUMP, which inhibits DNA synthesis and induces apoptosis.[5] Secondarily, 5-FUTP is incorporated into RNA, causing abnormal RNA processing, and, finally, 5-FdUTP is misincorporated into DNA, resulting in DNA strand breaks. The cytotoxicity of 5-FU is influenced by the levels of TS expression in tumor cells and the intracellular activity of dihydropyrimidine dehydrogenase (DPD), the primary and rate-limiting enzyme in the catabolism of 5-FU to inactive, but potentially toxic, metabolites.

LV is often used as biomodulator of 5-FU activity by stabilizing the 5-FU-TS complex, thus further inhibiting TS function. Compared with 5-FU alone, the combination of IV 5-FU and LV has been shown to increase RRs in colorectal cancer patients, although few studies have demonstrated a survival advantage.[6]

OFPs

Capecitabine is a fluoropyrimidine carbamate that is converted to 5-FU primarily in the liver by a 3-step enzymatic process: 1) carboxyesterase hydrolyzes capecitabine to 5'deoxy-5-fluorocytidine (5'-DFCR); 2) cytidine deaminase, an enzyme found in most tissues and tumors, converts 5'DFCR to 5'-deoxy-5-fluorouridine (5'-DFUR); and 3) thymidine phosphorylase (TP) hydrolyzes 5'-DFUR to the active drug 5-FU.[7] In addition to TS and DPD levels, tumor levels of TP

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largely influenced the antitumor efficacy of capecitabine. Because capecitabine is metabolized to 5-FU primarily in the liver, the gastrointestinal toxicities, primarily diarrhea, associated with oral 5-FU administration are minimized. Furthermore, certain tumors, including breast and colorectal tumors, contain larger amounts of TP than do corresponding nontumor-containing tissues, rendering these tumors more susceptible to capecitabine's cytotoxic action.

UFT is a combination of uracil and tegafur in a fixed molar ratio of 4:1. Tegafur is a pro-drug that is rapidly converted to 5-FU through cytochrome P450 (CYP-450) microsomes, TP, and spontaneous degradation.[8] Because 5-FU is rapidly inactivated by DPD, uracil, a competitive DPD inhibitor that inhibits the catabolism of 5-FU, is combined with tegafur to decrease the catabolism of 5-FU. When combined at equimolar dosages, UFT produces a 5-FU exposure profile comparable to that of CI 5-FU.[9] The antitumor activity of UFT is maximized when the uracil-to-tegafur molar ratio is 4:1.[10]

Eniluracil is a potent, irreversible DPD inhibitor. When combined with oral 5-FU, the plasma half-life and area under the curve of 5-FU are increased, mimicking that of CI 5-FU.[11] Following administration of eniluracil, 5-FU's half-life is 4 to 5 hours compared with 5 to 20 minutes following IV 5-FU administration. Renal clearance becomes the predominant route of elimination, necessitating dosage adjustment of this drug in patients with renal insufficiency.[12]

S1 is a combination of tegafur, 5-chloro-2,4-dihydroxypyridine (CDHP), and oxonic acid in a molar ratio of 1:0.4:1. CDHP is a potent but reversible inhibitor of DPD. Oxonic acid, is an inhibitor of 5-FU phosphorylation by the enzyme orotate phosphoribosyltransferase, which is found predominantly in the GI tract, but not in tumors.[13] As a result, the GI toxicities associated with orally administered 5-FU are significantly reduced. S1 is currently undergoing phase I and phase I/II trials in patients with advanced solid tumors.

Clinical Trials of OFPs

Because bolus and CI 5-FU have been used extensively to treat breast and colorectal cancers, studies have focused on OFP use in these diseases. Although UFT has been used in Japan for a long time, capecitabine is the only 5-FU analogue to be approved by the Food and Drug Administration (FDA), in 1998. It is indicated for patients with metastatic breast cancer (MBC) resistant to 1) paclitaxel and an anthracycline-based regimen or 2) paclitaxel, and who are not candidates for anthracycline regimens.[7] Bristol-Myers Squibb has recently submitted a marketing application to the FDA for UFT-LV as first-line treatment of colorectal cancer. Eniluracil is currently undergoing phase III trials in colorectal cancer and phase II trials in breast cancer.

Capecitabine

Breast Cancer

Two capecitabine phase II trials, the results of which are summarized in Table 1, have been conducted in MBC patients. The first was a multicenter trial that included 162 patients who had paclitaxel-refractory disease and had received a prior anthracycline regimen.[14] Patients must

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Table 1. Studies of Capecitabine in MBC Treatment

	Study 1[14]	Study 2[15]
No. of patients		
CR	3 pts	NA
Overall RR		
	(95% CI: 14-28%)	(95% CI: 13-35%)
Median duration of response		
Median TTP	3 mo	3.7 mo
MST		
Improved pain scores	47%	27.3%
Grade 3/4 diarrhea		
Grade 3/4 hand-foot syndrome	10%	18%
Grade 3/4 hematologic toxicity		

CI=confidence interval; CR=complete response; MBC=metastatic breast cancer; MST=median survival time; NA=not available; RR=response rate; TTP=time to disease progression.

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have received 2, but no more than 3 chemotherapy regimens, 1 of which contained paclitaxel as treatment for MBC. Patients received capecitabine 2,510 mg/m²/d in 2 divided doses for 14 days, followed by 7 days of rest. Cycles were repeated every 3 weeks. In a second multicenter trial, 74 patients with taxane-refractory (paclitaxel and docetaxel) MBC received capecitabine at 2,500 mg/m²/d given for 14 days, followed by 7 days of rest. Again, cycles were repeated every 3 weeks.[15] Patients had received at least 2, but no more than 3 prior chemotherapy regimens, 1 of which contained either paclitaxel or docetaxel. Results of both trials showed impressive activity and a favorable toxicity profile in taxane-refractory MBC (Table 1).

O'Shaughnessy et al[16] randomized 95 women 55 years of age or older to receive either cyclophosphamide, methotrexate, and 5-FU (CMF) every 21 to 28 days or capecitabine (2,510 mg/m²/d x 14 d) every 21 days as first-line treatment of MBC. Overall RRs in the capecitabine and CMF groups were 25% (confidence interval, 14%–37%) and 16% (confidence interval, 5%–33%), respectively. Median times to disease progression (TTP) were 132 and 94 days, respectively. Capecitabine-related side effects included grades 3 and 4 hand-foot syndrome (16%) and diarrhea (8%). The CMF regimen resulted in more hematologic toxicities (47%).

All of these studies used at least 2,500 mg/m²/d of capecitabine; however, a lower starting dose of 2,000 mg/m²/d may improve capecitabine's therapeutic index in MBC patients.[17] A retrospective analysis did not show a decrease in efficacy when dose intensity was reduced because of side effects.[18]

These study results show that capecitabine is an active drug in taxane- and anthracycline-refractory MBC. Docetaxel, paclitaxel, the anthracyclines, and paclitaxel-trastuzumab as first-line MBC therapy produce higher RRs than does capecitabine; however, these regimens are aggressive, warranting consideration of capecitabine instead. Combining capecitabine with other agents active in MBC will help to define its role as first-line therapy.

Colorectal Cancer

Two phase III trials have compared capecitabine with the Mayo Clinic 5-FU-LV regimen (5-FU 425 mg/m² plus LV 20 mg/m² d 1-5, q 28 d) in previously untreated advanced colorectal cancer patients (Table 2).[19,20] Overall, capecitabine results in higher RRs and a more favorable toxicity profile than 5-FU-LV.

Hand-foot syndrome and diarrhea occurred in 16% to 18% and 10% to 15% of capecitabine patients, respectively. Neutropenia (20%–26%), stomatitis (13%–16%), and diarrhea (10%–14%) were more common in the 5-FU-LV groups.

Table 2. Studies of Capecitabine vs 5-FU-LV in Advanced Colorectal Cancer

Study	Capecitabine* vs 5-FU-LV†
	Study 1[19] (N=602)
RR	26.6% vs. 17.9% (P=.013)
Duration of response	7.3 vs. 9.6 mo
PFS time	5.3 vs. 4.8 mo

*Capecitabine 2,500 mg/m²/d x 14 d, q 21 d.
†5-FU 425 mg/m² + LV 20 mg/m² d 1-5, q 28 d.
PFS=progression-free survival; RR=relapse rate.

UFT

Breast Cancer

Small trials have evaluated UFT as adjuvant and MBC therapy. As a single agent, UFT produces RRs ranging from 24% to 39%.[21] UFT-LV produced a 28% RR and UFT plus cyclophosphamide, doxorubicin and tamoxifen produced a 58% RR in heavily-pretreated MBC patients.[21,22] Studies of UFT combined with vinorelbine and paclitaxel in MBC patients are also underway. Larger trials are needed to define the role of UFT in MBC or adjuvant chemotherapy combinations.

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Colorectal Cancer

Results of numerous small phase I/II trials have shown that, when combined with LV 150 mg/d, UFT at 300 mg/m²/d for 28 days, with 1 or 2 weeks of rest, provides maximal dose intensity with an acceptable toxicity level.[9] In subsequent phase III studies, the LV dose was reduced to 75 to 90 mg/d because of LV's saturable oral bioavailability. The toxicity profile of UFT includes predominantly diarrhea, nausea and vomiting, fatigue and transient elevations in bilirubin levels. RRs in phase II trials ranged from 25% to 42%.[10]

Pazdur et al[23] conducted a pivotal phase III trial in which 816 patients with metastatic colorectal cancer were randomized to receive either UFT 300 mg/m² and LV 75 or 90 mg/d in 3 divided doses for 28 days followed by 7 days of rest or IV 5-FU 425 mg/m²/d plus LV 20 mg/d for 5 days. The oral regimen was repeated every 35 days, whereas the IV regimen was repeated every 28 days. RRs between the 2 regimens were not significantly different (12% vs 15%; P=.232), nor were median survival times (12.4 and 13.4 months, respectively).[24] Side effects of both treatments are summarized in Table 3.

Table 3. Side Effects of UFT-LV vs 5-FU-LV in a Phase III Trial of Metastatic Colorectal Cancer Patients

Type of Toxicity	Any Toxicity (CTC Grades 1–4)		P Value	Severe Toxicity (CTC Grades 3–4)		P Value
	UFT-LV	[redacted]		UFT-LV	[redacted]	
	No. of Patients (%)			No. of Patients (%)		
Diarrhea	27 (67)	[redacted]	.006	66 (23)	[redacted]	NS
Nausea/Vomiting	27 (67)	[redacted]	.020	53 (13)	[redacted]	NS
Mucositis	97 (24)	[redacted]	<.001	6 (1)	[redacted]	<.001
Neutropenia	52 (13)	[redacted]	<.001	3 (1)	[redacted]	<.001
Thrombocytopenia	84 (21)	[redacted]	<.001	0 (0)	[redacted]	.003
Anemia	33 (83)	[redacted]	NS	13 (3)	[redacted]	.032

CTC=National Cancer Institute Common Toxicity Criteria; NS=not significant.

Eniluracil

Eniluracil has been studied in combination with oral 5-FU in colorectal and breast cancers, squamous cell carcinoma of the head and neck, and other solid tumors. These studies evaluated different doses and schedules of each agent.

Breast Cancer

Results of small studies have shown that the combination of eniluracil and low-dose oral 5-FU is active and tolerable in MBC. In one study,[25] eniluracil 10 mg/m² and oral 5-FU 1 mg/m² was administered to 29 patients as first-line therapy twice daily for 28 days. Cycles were repeated every 35 days. The overall RR was 55% (confidence interval, 37%–73%) and the median duration of response was 14 months. Grade 3 neutropenia was the only hematologic toxicity to develop in 6% of patients. Grades 1 and 2 diarrhea and hand-foot syndrome were observed in 39% and 15% of patients, respectively.

Colorectal Cancer

Oral 5-FU 10 to 25 mg/m²/d combined with eniluracil was evaluated in colorectal cancer studies, resulting in the primary toxicity of moderate to severe neutropenia.[26,27] Goldberg et al[28] studied the combination of eniluracil 50 mg administered on days 1 to 7, with 5-FU 20 mg/m² given on days 2 to 6, repeated every 28 days in patients with metastatic colorectal cancer. The overall RR was 25% (95% confidence interval, 17%–37%). Median duration of response was 6.6 months, and median TTP was 5 months (95% confidence interval, 3.9–5.9 months). Grades 3 and 4 neutropenia were reported in 29% and 26% of patients, respectively. Other toxicities included cerebellar symptoms (6 patients), visual alterations (2 patients), and sensory, motor, or cortical symptoms (1 patient each).

These study results indicate the efficacy of eniluracil in combination with oral 5-FU in the treatment of breast and colorectal cancers. A large phase III trial is currently comparing eniluracil-5-FU to IV 5-FU-LV in advanced colorectal cancer.

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Future Directions

In addition to current studies of the OFP S1, at least one other OFP analogue—BOF-A2—is in development. Almost all of these new agents are being evaluated in combination with cisplatin or other active regimens in squamous cell cancer of the head and neck. Larger trials comparing 5-FU with the OFPs will validate the claim of improved QOL with the new oral agents. Finally, pharmacoeconomic analyses will determine the cost-effectiveness of these new and expensive drugs.

Conclusion

Results from studies of the OFP analogues demonstrate comparable, if not enhanced, efficacy compared with that of IV 5-FU. The standard of care for first-line treatment of advanced colorectal cancer was recently redefined as irinotecan-5-FU-LV, based on improved survival times when this combination was compared with 5-FU-LV. To define the role of the OFPs in colorectal cancer treatment, comparative studies of the OFPs with this new care standard are warranted. A better understanding of the pharmacokinetic and pharmacodynamic properties of this class of agents, administered alone or in combination with other cytotoxic agents, will enable practitioners to individualize therapy to maximize efficacy and minimize toxicity.

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ONCOLOGY THERAPEUTICS NETWORK

FDA UPDATES

RECENT FDA APPROVALS

New Indications for Chemotherapeutic Agents

In June 2000, the Food and Drug Administration (FDA) approved the use of tamoxifen (Nolvadex®, AstraZeneca) to reduce the risk of invasive breast cancer in women with ductal carcinoma in situ (DCIS) following breast surgery and radiation therapy. Tamoxifen is the first medication to be approved for DCIS. The FDA reviewed results of a pivotal trial reported by Fisher et al for the National Surgical Adjuvant Breast and Bowel Project (NSABP). The study randomized 1,804 women with DCIS who had undergone a lumpectomy and radiation therapy to either tamoxifen 20 mg daily for five years or placebo.[1] At a median follow-up of five years, the tamoxifen group had fewer breast cancer developments than did the placebo group (8.2% vs 13.4%, $P = .0009$). Other FDA-approved indications for tamoxifen include metastatic breast cancer treatment, adjuvant treatment of breast cancer, and reduction of breast cancer incidence in high-risk women. Side effects of tamoxifen include vaginal discharge, hot flashes, weight gain, skin rash, and thromboembolism.

Also in June 2000, paclitaxel (Taxol®, Bristol-Myers Squibb) received FDA approval for a shorter, 3-hour–administration regimen in combination with cisplatin as first-line treatment of advanced ovarian cancer. Paclitaxel is also approved as a 24-hour infusion when combined with cisplatin for this indication. Data supporting this indication came from a phase III trial of 680 patients with advanced ovarian cancer who were randomized to receive either 6 courses of paclitaxel 175 mg/m² over 3 hours followed by cisplatin (75 mg/m²) or 6 courses of cyclophosphamide (750 mg/m²) followed by cisplatin (75 mg/m²).[2] Both the median progression-free survival (PFS) and overall survival (OS) times were significantly prolonged in the paclitaxel-cisplatin group compared with the cyclophosphamide-cisplatin group (PFS: 15.5 months vs 11.5 months, $P = .0005$; OS: 35.6 months vs 25.8 months, $P = .0016$). Febrile neutropenia occurred in only 3% of treatment cycles in both groups. Furthermore, grade 3 and 4 neutropenia was higher in the cyclophosphamide-cisplatin group compared with the paclitaxel-cisplatin group (73% vs 64%). Other FDA-approved indications for paclitaxel include second-line, single-agent treatment of advanced ovarian carcinoma; adjuvant treatment of node-positive breast cancer; breast cancer treatment after failure of combination chemotherapy; first-line treatment, in combination with cisplatin, of non–small cell lung cancer; and second-line treatment of AIDS-related Kaposi's sarcoma. Side effects of paclitaxel include neutropenia, thrombocytopenia, anemia, peripheral neuropathy, myalgia, and hypersensitivity reactions.

Anticancer Orphan Drug Products

The FDA has recently granted orphan drug status to Arsenic Trioxide (Trisenox®, Cell Therapeutics, Inc) for an expanded indication — the treatment of myelodysplastic syndromes. Arsenic trioxide already has US orphan drug designation for the treatment of both multiple myeloma and refractory acute promyelocytic leukemia. At low doses, Aresenic Trioxide induces apoptosis through a mechanism different from that of the retinoids.

Generic Chemotherapeutic Agents

The Office of Generic Drugs of the FDA has approved applications for several chemotherapeutic agents. A 250-mg hydroxyurea capsule marketed by Duramed Pharmaceuticals has been approved, and the company plans to begin shipment by late summer. Also, Mylan Pharmaceuticals received approval to market its generic tamoxifen citrate 10-mg tablet.

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An Introduction to ORCA

ORCA (Oral Reimbursement for Cancer Agents) is a free service provided by Oncology Therapeutics Network (OTN), which can simplify and expedite billing and reimbursement for oral chemotherapy and supportive care medicines in your office.*

Why participate?

- Simplifies the use of oral therapies in the physician's office
- Eliminates concerns over reimbursement delays and denials
- Service is provided "free of charge" by OTN

How does ORCA work?

There are four components to the program:

1. Enrollment in the National Supplier Clearinghouse (NSC)
2. Drug fulfillment through OTN
3. Billing, collection, and appeals of individual claims through ORCA
4. Drug replacement is guaranteed if reimbursement is not approved

Which oral medications and insurance carriers are covered by ORCA?

- Cytoxan[2] Tablets (cyclophosphamide tablets, USP)
- VePesid[3] (etoposide) Capsules

The ORCA program covers all Medicare patients. It is expected that the program will be expanded in the near future to cover additional chemotherapeutic and supportive care medicines and additional insurance carriers.

Who is eligible to participate in ORCA?

Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

1. If you are not already an OTN customer, call 1-800-482-6700 to set up an account.
2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices

ORCA™

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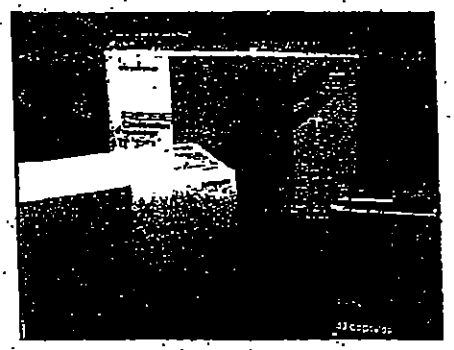
A combination of Rebetol (Ribavirin, USP) Capsules and Intron® A (Interferon alfa-2b, recombinant) indicated for the treatment of chronic hepatitis C in patients who have relapsed following alpha interferon therapy.



ONCOLOGY THERAPEUTICS NETWORK

Schering®

CATALOG NUMBER	NDC#	BRAND NAME	ITEM			
220-300	0085-1241-01	Rebetron	Interferon alpha-2b/Ribavirin 1200/Pak 3	3 MIU/0.5 mL	$676.98	$755.70
220-310	0085-1236-01	Rebetron	Interferon alpha-2b/Ribavirin 1200 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$676.98	$755.70
220-320	0085-1241-02	Rebetron	Interferon alpha-2b/Ribavirin 1000/Pak 3	3 MIU/0.5 mL	$612.95	$683.89
220-330	0085-1236-02	Rebetron	Interferon alpha-2b/Ribavirin 1000 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$612.95	$683.89
220-340	0085-1241-03	Rebetron	Interferon alpha-2b/Ribavirin 600/Pak 3	3 MIU/0.5 mL	$501.69	$560.09
220-350	0085-1236-03	Rebetron	Interferon alpha-2b/Ribavirin 600 MDV	22.8 MIU/3.8 mL; 3 MIU/0.5 mL	$501.69	$560.09

REIMBURSEMENT

Average Wholesale Prices and 2000 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alphabetically by their generic name. The AWPs are obtained from the *2000 Red Book* and updates. For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the next two columns. Please refer to the *Sourcebook* for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Proleukin®						
Aldesleukin	22 MIU		645.00		per 22 MIU	
Ethyol®						
• Amifostine	500 mg		387.50		500mg	
Fungizone®						
• Amphotericin B Oral Susp	25 ml		27.10			
Blenoxane®						
Bleomycin Sulfate, pwd	15 Units		304.60		15 units	
Bleomycin Sulfate, pwd	30 Units		609.20		15 units	
Xeloda®						
Capecitabine 150mg Tablet	120 Tabs		259.55		150mg	
Capecitabine 500mg Tablets	240 Tabs		1,730.24		500mg	
Paraplatin®						
Carboplatin, pwd	50 mg		109.31		50mg	
Carboplatin, pwd	150 mg		327.93		50mg	
Carboplatin, pwd	450 mg		983.75		50mg	
BiCNU®						
Carmustine, pwd	100 mg		114.69		100mg	

ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Platinol®-AQ						
Cisplatin 1mg/ml, inj	50 ml MDV		249.98		50mg	
Cisplatin 1mg/ml, inj	100 ml MDV		499.91		50mg	
Leustatin®						
Cladribine 1mg/ml, inj	10 ml		562.80		1mg	
Cytogam®						
Cytomegalovirus Immune Globulin	50 ml		690.81		Per vial	
Cytoxan® lyophilized						
Cyclophosphamide lyopholized	100 mg		6.45		100mg	
Cyclophosphamide lyopholized	200 mg		12.25		200mg	
Cyclophosphamide lyopholized	500 mg		25.71		500mg	
Cyclophosphamide lyopholized	1 Gram		51.43		1 Gram	
Cyclophosphamide lyopholized	2 Gram		102.89		2 Gram	
Cytoxan® Tablets						
Cyclophosphamide 25mg Tablet	100 Tabs		235.21		25mg	
Cyclophosphamide 50mg Tablet	100 Tabs		431.66		25mg	
Cyclophosphamide 50mg Tablet	1000 Tabs		4,111.35		25mg	
Cytarabine pwd	100 mg		6.25		100mg	
Cytarabine pwd	500 mg		25.71		500mg	
Cytarabine pwd	1 Gram		50.15		500mg	
Cytarabine pwd	2 Gram		100.28		500mg	
DTIC-Dome®						
Dacarbazine, pwd	200 mg		27.73		200mg	
DaunoXome®						
Daunorubicin citrate liposome 2mg/ml inj	25 ml		340.00		10mg	
Cerubidine®						
Daunorubicin HCl, pwd	20 mg		168.50		10mg	
DDAVP®						
Desmopressin Acetate 4mcg/ml	1 ml		26.67		1 mcg	
Zinecard™						
• Dexrazoxane, pwd	250 mg		178.06		250mg	
• Dexrazoxane, pwd	500 mg		356.10		250mg	
Diphenhydramine HCl 50mg/ml inj.	1 ml		1.24		Up to 50mg	
Taxotere®						
Docetaxel 20mg/0.5ml, inj	0.5 ml SDV		298.58		20mg	
Docetaxel 20mg/0.5ml	2 ml SDV		1,194.30		20mg	
Anzemet®						
Dolasetron 20mg/ml, inj	5 ml		166.50		10mg	
Rubex®						
Doxorubicin HCl, pwd	50 mg		197.15		10mg	
Doxorubicin HCl, pwd	100 mg		394.29		10mg	
Doxorubicin HCl, pwd	10 mg		45.08		10mg	
Doxorubicin HCl, pwd	20 mg		90.16		10mg	
Doxorubicin HCl, pwd	50 mg		225.40		10mg	
Doxorubicin HCl 2mg/ml, inj	5 ml		47.35		10mg	
Doxorubicin HCl 2mg/ml, inj	10 ml		94.70		10mg	
Doxorubicin HCl 2mg/ml, inj	25 ml		236.74		10mg	
Doxorubicin HCl 2mg/ml, inj	100 ml		945.98		10mg	
Adriamycin™						
Doxorubicin RDF, pwd	10 mg		53.64		10mg	
Doxorubicin RDF, pwd	50 mg		268.18		10mg	
Doxorubicin RDF, pwd	150 mg		783.44		10mg	
Doxorubicin HCl pfs 2mg/ml, inj	5 ml		56.34		10mg	
Doxorubicin HCl pfs 2mg/ml	10 ml		112.66		10mg	
Doxorubicin HCl pfs 2mg/ml	25 ml		281.68		10mg	
Doxorubicin HCl pfs 2mg/ml	37.5 ml		422.51		10mg	
Doxorubicin HCl pfs 2mg/ml	100 ml		1,104.13		10mg	
Doxil®						
Doxorubicin, HCl liposome 2mg/ml inj	10 ml		708.25		10mg	
Procrit®						
• Epoetin Alpha 2000u/ml inj	1 ml		24.97		1,000units	
Epoetin Alpha 3000u/ml inj	1 ml		37.46		1,000units	
Epoetin Alpha 4000u/ml inj	1 ml		49.87		1,000units	
Epoetin Alpha 10, 000u/ml inj	1 ml		124.68		1,000units	
Epoetin Alpha 20, 000u/ml inj	1 ml		249.36		1,000units	
Epoetin Alpha 40, 000u/ml inj	1 ml		498.72		1,000units	

REIMBURSEMENT

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PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
VePesid®						
Etoposide 50mg Capsule	20 caps	00015-3078-45	1,020.54		50mg	
Etoposide 20mg/ml, inj	5 ml	00015-3085-20	136.49		100mg	
Etoposide 20mg/ml, inj	7.5 ml	00015-3084-20	204.74		100mg	
Etoposide 20mg/ml, inj	25 ml	00015-3061-20	665.38		100mg	
Etoposide 20mg/ml, inj	50 ml	00015-3062-20	1,296.64		100mg	
Etopophos®						
• Etoposide Phosphate, pwd	100 mg	00015-3404-20	124.14		100mg	
Fludara®						
Fludarabine Phosphate, pwd	50 mg	50419-0511-06	259.50	J9185	50mg	
Adrucil®						
Fluorouracil 50mg/ml, inj	10 ml	00013-1036-91	3.20	J9190	500mg	
Fluorouracil 50mg/ml, inj	50 ml	00013-1046-94	16.04	J9190	500mg	
Fluorouracil 50mg/ml, inj	100 ml	00013-1056-94	32.06	J9190	500mg	
Neupogen®						
• Filgrastim(G-CSF) 300mcg/ml, inj	300 mcg	55513-0530-01	180.40	J1440	300mcg	
• Filgrastim(G-CSF) 300mcg/ml, inj	480 mcg	55513-0546-01	287.40	J1440	480mcg	
• Amgen 300mcg/ml, inj	1 ml	55513-0530-10	180.40	J1440	480mcg	
• Amgen 300mcg/ml, inj	1 ml 10s	55513-0530-10	1,804.00	J1440	480mcg	
• Amgen 300mcg/ml, inj	1.600 ml	55513-0546-01	287.40	J1440	480mcg	
• Amgen 300mcg/ml, inj	1.600 ml 10s	55513-0546-10	2,874.00	J1440	480mcg	
Gemzar®						
• Gemcitabine HCl, pwd	200 mg	00002-7501-01	99.55	J9201	200mg	
Gemcitabine HCl, pwd	1 Gram	00002-7502-01	497.72	J9201	200mg	
Leukine®						
• Sargramostin(GM-CSF), pwd	250 mcg	58406-0002-01	144.30	J2820	50mcg	
• Sargramostin(GM-CSF) 500mcg/ml, inj	1 ml	58406-0003-01	288.59	J2820	50mcg	
Zoladex®						
Goserelin Acetate, implant	3.6 mg syringe	00310-0950-51	469.99	J9202	3.6mg	
Goserelin Acetate, implant	10.8 mg syringe	00310-0951-30	1,409.98	J9202	3.6mg	
Kytril®						
Granisetron HCl 1mg/ml, inj	1 ml	00029-4104-01	195.20	J2405	100mcg	
Granisetron HCl 1mg/ml, inj	4 ml	00029-4105-01	780.80	J2405	100mcg	
Ifex®						
Ifosfamide pwd	1 Gram	00015-3274-20	157.04	J9208	1gm	
Ifosfamide pwd	3 Gram	00015-3275-20	471.13	J9208	1gm	
Ifex®/Mesnex™						
Ifosfamide(10x1g)/Mesna(10x1g MDV)	Combo-Pack	00015-3276-20	2,610.16	J9208/J9209	1gm/200mg	
Ifosfamide(2x3g)/Mesna(6x1g MDV)	Combo-Pack	00015-3277-20	1,566.03	J9208/J9209	1gm/200mg	
Ifosfamide(5x1g)/Mesna(3x1g MDV)	Combo-Pack	00015-3278-20	1,080.21	J9208/J9209	1gm/200mg	
Venoglobulin S						
Immune Globulin 50mg/ml, inj w/IV set	50 ml	00002-7507-01	225.00	J1566	500mg	
Immune Globulin 50mg/ml, inj w/IV set	100 ml	00002-7508-01	450.00	J1566	500mg	
Immune Globulin 50mg/ml, inj w/IV set	200 ml	00002-7509-01	900.00	J1566	500mg	
Immune Globulin 100mg/ml, inj w/IV set	50 ml	00002-7510-01	475.00	J1566	500mg	
Immune Globulin 100mg/ml, inj w/IV set	100 ml	00002-7511-01	950.00	J1566	500mg	
Immune Globulin 100mg/ml, inj w/IV set	200 ml	00002-7512-01	1,900.00	J1566	500mg	
Gamimune®						
Immune Globulin 100mg/ml, inj	10 ml	00026-0610-20	90.00	J1566	500mg	
Immune Globulin 100mg/ml, inj	50 ml	00026-0611-20	450.00	J1566	500mg	
Immune Globulin 100mg/ml, inj	100 ml	00026-0612-20	900.00	J1566	500mg	
Immune Globulin 100mg/ml, inj	200 ml	00026-0613-20	1,800.00	J1566	500mg	
Polygam®						
Immune Globulin, pwd	2.5 Gram	00044-3000-02	223.75	J1566	5Grams	
Immune Globulin, pwd	5 Gram	00044-3000-05	447.50	J1566	5Grams	
Immune Globulin, pwd	10 Gram	00044-3000-10	895.00	J1566	5Grams	
WinRho®						
RHO (d) Immune Globulin, pwd	600 IU	00002-7503-01	142.00	J2790	100 IU	
RHO (d) Immune Globulin, pwd	1500 IU	00002-7504-01	324.50	J2790	100 IU	
RHO (d) Immune Globulin, pwd	5000 IU	00002-7505-01	1,081.50	J2790	100 IU	
Intron®-A						
• Interferon Alpha 2B 3MIU/0.5ml	3 MIU PAK	00085-1104-01	38.12	J9213	1 MIU	
• Interferon Alpha 2B 5MIU/0.5ml	5 MIU PAK	00085-1105-01	63.54	J9213	1 MIU	
Interferon Alpha 2B 10MIU/ML	10 MIU PAK	00085-1106-01	127.08	J9213	1 MIU	
Interferon Alpha 2B 6MIU/ml, inj	18 MIU MDV	00085-1140-01	228.72	J9213	1 MIU	
Interferon Alpha 2B 10MIU/ML, inj	25 MIU	00085-1142-01	317.70	J9213	1 MIU	

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REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Interferon Alpha 2B, pwd	5 MIU		63.53		1 MIU	
Interferon Alpha 2B, pwd	10 MIU		127.07		1 MIU	
Interferon Alpha 2B, pwd	18 MIU		228.72		1 MIU	
Interferon Alpha 2B, pwd	25 MIU		317.70		1 MIU	
Interferon Alpha 2B, pwd	50 MIU		635.36		1 MIU	
Roferon® A						
Interferon Alpha 2A 3MIU/ML, Inj	3 MIU		34.97		3 MIU	
Interferon Alpha-2A 6MIU/ml, inj	6 MIU		69.91		3 MIU	
Interferon Alpha 2A 9MIU/0.9ml, Inj	9 MIU		98.44		3 MIU	
Interferon Alpha 2A 6MIU/ml, Inj	18 MIU		209.60		3 MIU	
Interferon Alpha 2A 36MIU/ml, inj	36 MIU		419.26		3 MIU	
Camptosar®						
Irinotecan HCl 20mg/ml, Inj	2 ml		248.03		20mg	
Irinotecan HCl 20mg/ml, inj	5 ml		620.09		20mg	
Leucovorin®						
Leucovorin Calcium, pwd	50 mg		18.44		50mg	
Leucovorin Calcium, pwd	100 mg		35.00		50mg	
Leucovorin Calcium, pwd	200 mg		78.00		50mg	
Leucovorin Calcium, pwd	350 mg		137.54		50mg	
Lupron®						
Leuprolide Acetate, pwd	7.5 mg		623.79		7.5mg	
Leuprolide Acetate, pwd	22.5 mg		1,871.37		7.5mg	
Ativan®						
• Lorazepam 2mg/ml, Inj	1 ml		10.39		2mg	
• Lorazepam 2mg/ml, Inj	10 ml		59.64		2mg	
• Lorazepam 4mg/ml, inj	10 ml		74.57		2mg	
Mannitol®						
Mannitol 25%, inj	50 ml		6.13		50ml	
Mustargen®						
• Mechlorethamine HCl, pwd	10 mg		12.05		10mg	
Megace®						
Megestrol Acetate 20mg Tablet	100 tabs		75.68			
Megestrol Acetate 40mg Tablet	100 tabs		134.96			
Megestrol Acetate 40mg Tablet	250 tabs		330.68			
Megestrol Acetate 40mg Tablet	500 mg tabs		647.88			
Megestrol Acetate oral susp 40mg/ml	240 ml		154.04			
Alkeran®						
Melphalan HCl, pwd	50 mg		382.61		50mg	
Melphalan 2mg Tablet	50 tabs		109.23		2mg	
Mesnex™						
Mesna 100mg/ml, inj	10 ml		202.74		200mg	
Methotrexate®						
Methotrexate Sodium, pwd	20 mg		5.03		5mg	
Methotrexate Sodium, pwd	1 Gram		61.44		50mg	
Methotrexate Sodium 25mg/ml, Inj	2 ml		6.88		50mg	
Methotrexate Sodium 25mg/ml, Inj	4 ml		8.75		50mg	
Methotrexate Sodium 25mg/ml, Inj	8 ml		17.50		50mg	
Methotrexate Sodium 25mg/ml, Inj	10 ml		26.88		50mg	
Methotrexate Sodium 25mg/ml, Inj	2 ml		4.75		50mg	
Methotrexate Sodium 25mg/ml, Inj	10 ml		20.48		50mg	
Methotrexate Sodium 2.5mg Tablet	100 tabs		362.95		2.5mg	
Methotrexate Sodium 2.5mg Tablet	36 tabs		130.05		2.5mg	
Mutamycin®						
Mitomycin, pwd	5 mg		134.11		5mg	
Mitomycin, pwd	20 mg		452.91		20mg	
Mitomycin, pwd	40 mg		915.09		40mg	
Novantrone®						
Mitoxantrone HCl 2mg/ml, Inj	10 ml		939.04		5mg	
Mitoxantrone HCl 2mg/ml, Inj	12.5 ml		1,173.76		5mg	
Mitoxantrone HCl 2mg/ml, Inj	15 ml		1,408.55		5mg	
Sandostatin®						
Octreotide Acetate 50mcg/ml, Inj	1 ml		6.61			
Octreotide Acetate 100mcg/ml, Inj	1 ml		12.83			
Octreotide Acetate 500mcg/ml, Inj	1 ml		61.86			

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PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Sandostatin LAR® Depot						
Octreotide Acetate, pwd	10 mg		1,422.13		1mg	
Octreotide Acetate, pwd	20 mg		1,422.13		1mg	
Octreotide Acetate, pwd	30 mg		2,133.19		1mg	
Zofran®						
Ondansetron HCL 2mg/ml, Inj	20 ml		256.40		1mg	
Ondansetron HCL 2mg/ml, Inj	2 ml		25.64		1mg	
Ondansetron 32mg/50ml, premixed bag	50 ml		206.41		1mg	
Neumega®						
Oprelvekin, pwd	5 mg		248.75		5mg	
Taxol®						
Paclitaxel 6mg/ml, Inj	30 mg		182.63		30mg	
Paclitaxel 6mg/ml, Inj	100 mg		608.76		30mg	
Paclitaxel 6mg/ml, Inj	300 mg		1,826.25		30mg	
Aredia®						
Pamidronate disodium pwd	30 mg		266.54		30mg	
Pamidronate disodium pwd	90 mg		738.68		30mg	
Nipent™						
Pentostatin pwd	10 mg		1,645.00		10mg	
Compazine®						
Prochlorperazine 5mg/ml, Inj	10 ml		41.00		Upto10mg	
Prochlorperazine 10mg tab	100 tabs		94.50		10mg	
Zantac®						
Ranitidine 25mg/ml, Inj	2 ml		3.99		25mg	
Respigam®						
Respiratory Syncytial Virus Immune globul	20 ml		450.50		50mg	
Respiratory Syncytial Virus Immune globul	50 ml		755.15		50mg	
Rituxan™						
• Rituximab 10mg/ml, Inj	10 ml		464.53		100mg	
• Rituximab 10mg/ml, Inj	50 ml		2,322.68		100mg	
Zanosar®						
• Streptozocin, pwd	1 Gram		123.83		1Gram	
Vumon®						
Teniposide 10mg/ml, inj	5 ml		216.86		50mg	
Thioplex®						
Thiotepa, pwd	15 mg		112.96		15mg	
Hycamtin™						
Topotecan, pwd	3 mg		634.15		4mg	
Topotecan, pwd	4 mg, 5's		3,170.75		4mg	
Herceptin®						
Trastuzumab, pwd	440 mg		2,375.63		10mg	
Neutrexin®						
Trimetrexate, pwd	25 mg, 10's		825.00		25mg	
Trimetrexate, pwd	25 mg, 50's		4,125.00		25mg	
Trimetrexate, pwd	200 mg		660.00		25mg	
Urokinase®						
Urokinase, pwd	5000 IU		59.59		5000IU	
Urokinase, pwd	9000 IU		103.91		5000IU	
Velban®						
Vinblastine sulfate pwd	10 mg		21.25		1mg	
Vinblastine sulfate 1mg/ml, Inj	10 ml		43.23		1mg	
Vincristine®						
Vincristine sulfate 1mg/ml, inj	1 ml		43.23		1mg	
Vincristine sulfate 1mg/ml, inj	1 ml		31.75		1mg	
Vincristine sulfate 1mg/ml, inj	2 ml		86.46		2mg	
Vincristine sulfate 1mg/ml, Inj	2 ml		38.25		2mg	
Navelbine®						
Vinorelbine 10mg/ml, Inj	1 ml		79.48		10mg	
Vinorelbine 10mg/ml, Inj	5 ml		397.38		10mg	

• An AWP, HCPCS code or NDC that has changed or been added has been highlighted in color.

* The drug code J9999 is defined as "not otherwise classified, antineoplastic drug." The Health Care Financing Administration (HCFA) has not assigned specific codes to these drugs.

† The drug code J3490 is defined as "unclassified drug." These drugs may or may not be defined as an unclassified drug in your area. Consult your local carrier for the appropriate code.

‡ Q0136 is the code for non-ESRD (End Stage Renal Disease) use.

+ J2405 should be used for all formulations of Zofran.

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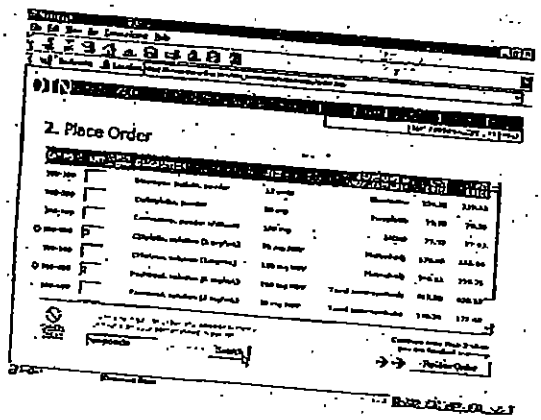

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Oncology Therapeutics Network
395 Oyster Point Blvd., Suite 405
So. San Francisco, CA 94080.

ONCOLOGY THERAPEUTICS NETWORK

August 2000

OTN THE NETWORK NEWS

ONCOLOGY THERAPEUTICS NETWORK

AN UPDATE FOR COMMUNITY-BASED ONCOLOGY PROFESSIONALS

Route To:
- ☐ Physician
- ☐ Office Manager
- ☐ Oncology Nurse
- ☐ Pharmacist
- ☐ Business Office
- ☐ _____

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Highlights*†

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REIMBURSEMENT ASSISTANCE

Bobbi Buell, MBA
President, Documedics

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99211 "Nurse Only" Q&A

Q: *Is it true that an office can bill 99211 with every chemotherapy?*

A: According to the original Physician Fee Schedule for Medicare patients published on 11/25/91, ONE Evaluation and Management service (99201-99215) can be billed with every chemotherapy for Medicare patients. This is because, whether or not the physician physically sees the patient, physician work is involved with every chemo. Since there are no WORK relative values paid by Medicare for chemotherapy administration (96400-96412), visits are separately payable. The Medicare Carriers' Manual Section 15400(D) states that: "On days when the physician has no face-to-face contact with the patient, the physician may report and be paid for "incident to" services furnished by one of the physician's employees, in addition to the chemotherapy administration, if they are furnished under direct personal supervision in the office by one of the physician's employees and the medical records reflect the physician's active participation in and management of the course of treatment." 99211 for Nursing intervention can be billed, if no other E/M service is billed that day. Additionally, CPT states that "If significantly separately identifiable Evaluation and Management service is performed, the appropriate E/M service should be reported in addition to 96400-96549." All insurance companies should abide by these standards if documentation and coding requirements are met. The practice's responsibility is to ensure that all insurance contracts have a clause that obligates the payer to adhere to CPT standards.

Q: *What are the documentation guidelines for 99211? Have they changed?*

A: Unlike for other Evaluation and Management services, there are no official guidelines for 99211 from either the American Medical Association or from the Healthcare Financing Administration (HCFA). However, there have been a number of pre-payment audits of Oncology practices where Medicare discovered that there was no documentation of nursing intervention and/or interaction with the treating physician. Medicare denied payment for lack of documentation. A few years ago, ASCO requested guidelines from HCFA. These guidelines state that the nurse must document interaction with and supervision by the treating physician. For example, the nurse may write a note that states: "Reviewed CBC with Dr. Doe, he said to give chemotherapy per the order dated 6/9/98." These guidelines are more restrictive for Oncology than for other specialties and ASCO has requested that HCFA re-evaluate these guidelines. So far, HCFA has not done so. Until this re-evaluation occurs, documentation must be consistent with the interaction and supervision of nurses by the physician.

Q: *Does the physician need to be in the office for 99211 to be billed to Medicare?*

A: In most cases, the physician must be in the office suite for 99211 to be billed. However, if State licensing allows for Nurse Practitioners to treat independently, Nurse Practitioners and/or Physician Assistants may bill Evaluation and Management services under their own provider number. This only pays 85% of the physician fee schedule. When the physician is in the office suite, 100% of the physician fee schedule will be paid. In addition, anyone for whom 99211 is billed should be a leased or paid full-time employee of the practice.

Q: *Should we bill 99211 with every injection of non-chemo drugs given in the office?*

A: This depends upon the interaction with the physician and nursing activities performed. Whenever an injection of non-chemo drugs, such as epoetin alfa (EPO) or growth factors, is given, there is a billing choice between a therapeutic injection (90782) and 99211. Both are not paid by MOST insurance companies when billed the same day. If all that is done for the patient is an injection, use 90782. If the nurse interacts with the physician regarding patient treatment and/or performs other nursing interventions for the patient, 99211 can be billed, if this is well documented AND is medically necessary. Pre-payment audit rejections can occur, if all that is documented is a 'drive-by shooting.' Or, if a Carrier sees that 99211s are billed every day, this can send up a 'red flag' for medical necessity.

Q: *Can dietitians, social workers, or medical assistants use 99211? Can they bill to higher levels of Evaluation and Management services?*

A: ANY employee in a physician's office providing patient care may bill 99211. Be aware that there are no codes that are regularly paid for patient teaching or counseling by non-physician practitioners. 99211 is the only code that can be predictably paid for these activities despite counseling or teaching codes listed in CPT. Billing to higher levels of Evaluation and Management services not permitted, except for Nurse Practitioners, Clinical Nurse Specialists and/or Physicians' Assistants. Depending upon state licensing, these practitioners can bill under their own provider numbers or 'incident to' physician services. We do not recommend, however, that non-physician practitioners bill any Evaluation and Management service where high complexity decision-making required.

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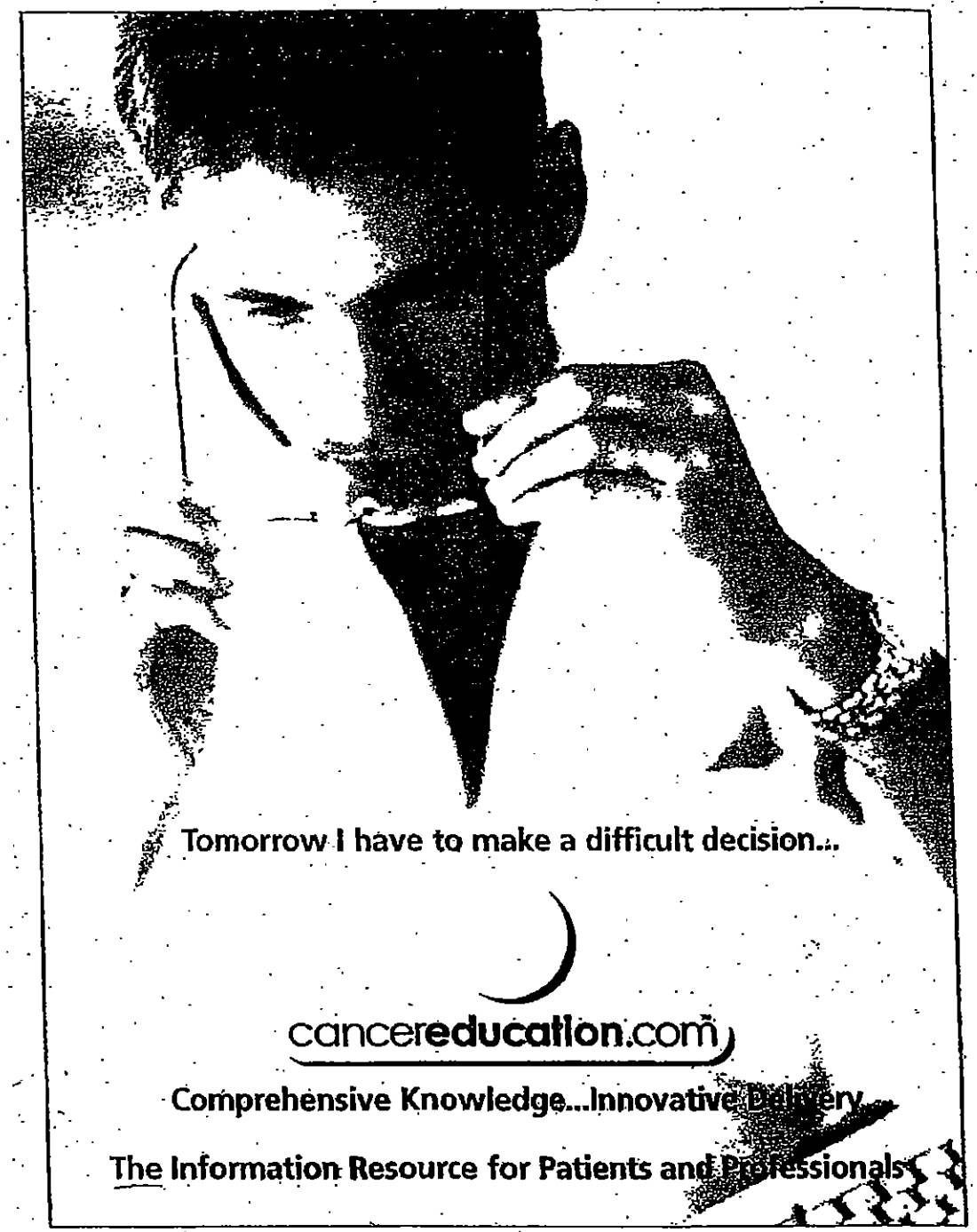

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A Program Supporting the Reimbursement of Oral Chemotherapy and Supportive Care Medicines in Physician Offices

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An Introduction to ORCA

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4. Drug replacement is guaranteed if reimbursement is not approved

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Who is eligible to participate in ORCA?

Any office-based physician practice is eligible to participate in the ORCA program.

How do I enroll in the program?

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2. Once you have set up an account, or if you are already an OTN customer, call the ORCA program at 1-877-SAY-ORCA (1-877-729-6722) to request an enrollment packet.

* The ORCA program is a free service provided by OTN and is administered by AccessMED, 6900 College Boulevard, Suite 1000, Overland Park, KS 66211. AccessMED is a leading reimbursement and consulting firm focused on oncology.

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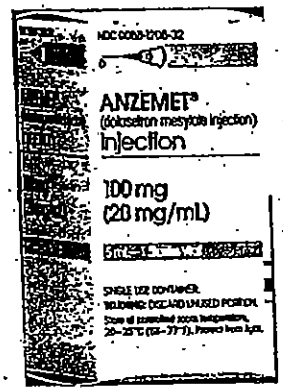

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970-300	0088-1203-05	Anzemet	dolasetron mesylate	100 mg tablets	5	$343.20
970-305	0088-1203-29	Anzemet	dolasetron mesylate	100 mg tablets blister pack	5	$686.40
970-310	0088-1203-43	Anzemet	dolasetron mesylate	100 mg tablets unit dose	10	$686.40

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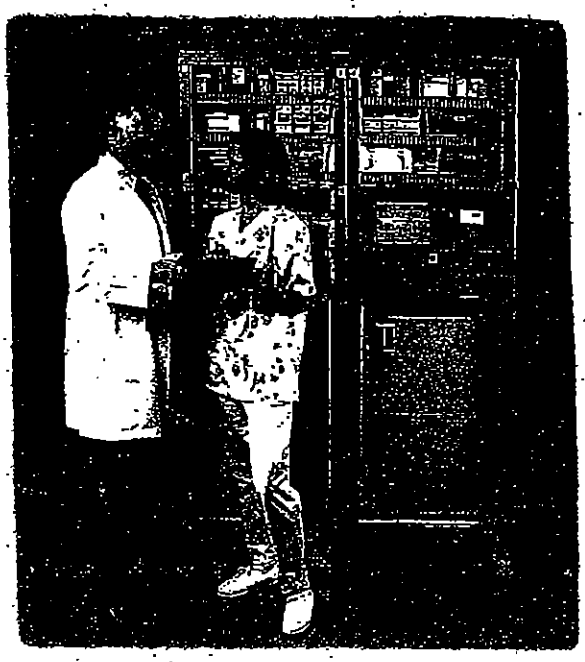

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ONCOLOGY DRUG UPDATES

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Antiemetics in the Oncology Patient:
A Comparison of Published Clinical Practice Guidelines

Amy W. Valley, PharmD, BCOP

Introduction

Nausea and vomiting (N/V) are among the most dreaded side effects of cancer chemotherapy.[1] Uncontrolled N/V can result in several adverse consequences, including dehydration, malnutrition, electrolyte derangement, and tearing of the gastrointestinal mucosa; additionally, patients may refuse to undergo further chemotherapy. Unsurprisingly, these consequences have proved to impair the quality of life in cancer patients.[2] The psychological consequences of uncontrolled N/V may range from mild anxiety to the development of severe anticipatory N/V. Although N/V is usually associated with chemotherapy, radiation therapy is also known to cause N/V, which can also be severe.

On a positive note, the past two decades have brought advances in the understanding of the physiology of emesis, resulting in the development of the serotonin (5-HT_3)-receptor antagonists. These potent antiemetics have reshaped the delivery of chemotherapy and resulted in an explosion of research regarding emesis control. Several groups have recently developed antiemetic guidelines to 1) summarize the large body of published literature and 2) define the standard of care in prevention of N/V in cancer patients. This article compares the published antiemetic guidelines issued by the following organizations: The National Comprehensive Cancer Network (NCCN), the Multinational Association of Supportive Care in Cancer (MASCC), the American Society of Health-System Pharmacists (ASHP), and the American Society of Clinical Oncology (ASCO).[3-6] Table 1 summarizes general background features.

Continued on next page

Table 1. *General Guideline Comparison*

Guideline Feature	Organization			
	ASCO	MASCC	NCCN	ASHP
Composition of expert panel	Multidisciplinary	Multidisciplinary	Multidisciplinary	Physicians only
Rigorous, evidence-based guideline?	Yes	Yes	No	No
Method of grading the strength of the recommendation	Based on type (I-V)* and level of evidence (A-D)†	Based on 4 levels of evidence (A-D)‡	Based on 3 levels of evidence (category 1-3)§	Based on 3 levels of consensus & confidence (low-high)¶
Publication date	9/99	4/99	11/97	9/98
Focus	Chemotherapy, RT	Chemotherapy, RT, post-surgery	Chemotherapy, RT	Chemotherapy, RT

*Level I: Evidence is obtained from meta-analysis of multiple, well-designed, controlled studies. Randomized trials have low false-positive and low false-negative errors (high power); Level 2: Evidence is obtained from at least 1 well-designed experimental study. Randomized trials have high false-positive and/or -negative errors (low power); Level III: Evidence is obtained from well-designed, quasi-experimental studies such as nonrandomized, controlled, single-group, pre-post, cohort, time, or matched case-control series; Level IV: Evidence is from well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies; Level 5: Evidence is from case reports and clinical examples.

†A: There is evidence of type I or consistent findings from multiple studies of types II, III, and IV. B: There is evidence of types II, III, and IV, and findings are generally consistent; C: There is evidence of types II, III, and IV, but findings are inconsistent; D: There is little or no systematic empirical evidence.

‡A: Strong research-based evidence (multiple relevant and high-quality scientific studies); B: moderate research-based evidence (one relevant, high-quality scientific study or multiple adequate scientific studies; C: Limited research-based evidence (at least one adequate scientific study in patients with nausea and vomiting, published in a reputable medical journal; D: Panel interpretation of information that did not meet inclusion criteria as research-based evidence.

§Category 1: Recommendations that are uncontested and generally accepted by all authorities in that particular cancer; Category 2: Recommendations that are somewhat controversial; Category 3: Recommendations that caused real disagreements among members of the NCCN panel.

¶"The level of scientific confidence was classified as: 1) high when a number of well-conducted randomized controlled trials of appropriate size were available; 2) moderate when at least 1 randomized clinical trial supported by well-conducted phase II trials was available; and 3) low when formal clinical trials were of a level less that that expressed in the high and moderate categories, and "no confidence possible".

ASCO=American Society of Clinical Oncology; ASHP=American Society of Health-System Pharmacists; MASCC=Multinational Association of Supportive Care in Cancer; NCCN= National Comprehensive Cancer Network; RT= radiation therapy.

Table 2. *Classification of Emetogenic Risk*

High	*High Cisplatin (>99% risk)* Cisplatin	*Level 5 (> 90% risk)* carmustine (> 250 mg/m²), cisplatin (@ 50 mg/m²), cyclophosphamide (> 1,500 mg/m²), dacarbazine (@ 500 mg/m²), lomustine (> 60 mg/m²), mechlorethamine, pentostatin, streptozocin	*Level 5 (> 90% risk)* carmustine (> 250 mg/m²), cisplatin (@ 50 mg/m²), cyclophosphamide (> 1,500 mg/m²), dacarbazine, mechlorethamine, streptozocin.	*High (> 90% risk)* carmustine (> 250 mg/m²), cisplatin (@ 50 mg/m²), cyclophosphamide (> 1,500 mg/m²), dacarbazine, mechlorethamine, streptozocin
Moderately High	*Noncisplatin (30%–90% risk)* *listed in order of decreasing risk:* dacarbazine, dactinomycin, mechlorethamine, streptozocin, hexamethylmelamine, carboplatin, cyclophosphamide, lomustine, carmustine, daunorubicin, doxorubicin, epirubicin, idarubicin, cytarabine, ifosfamide	*Level 4 (60%–90% risk)* carboplatin, carmustine (< 250 mg/m²), cisplatin (< 50 mg/m²), cyclophosphamide (751–1,500 mg/m²), cytarabine (@ 1 gm/m²), dactinomycin (> 1.5 mg/m²), doxorubicin (> 60 mg/m²), irinotecan, melphalan (IV), methotrexate (@ 1,000 mg/m²), mitoxantrone (> 15 mg/m²), procarbazine	*Level 4 (60%–90% risk)* carboplatin, carmustine (≤ 250 mg/m²), cyclophosphamide (751–1,500 mg/m²), cytarabine (> 1 gm/m²), doxorubicin (> 60 mg/m²), methotrexate (@ 1,000 mg/m²), procarbazine	*Moderate-High (30%–90% risk)* carboplatin, carmustine (≤ 250 mg/m²), cisplatin (< 50 mg/m²), cyclophosphamide (< 1,500 mg/m²), oral cyclophosphamide, cytarabine (> 1 gm/m²), doxorubicin, epirubicin, hexamethylmelamine, ifosfamide, irinotecan, methotrexate (> 250 mg/m²), mitoxantrone, procarbazine, topotecan
Moderate		*Level 3 (30%–60% risk)* aldesleukin, cyclophosphamide (≤ 750 mg/m²), dactinomycin (≤ 1.5 mg/m²), doxorubicin (20–60 mg/m²), epirubicin (≤ 90 mg/m²), idarubicin, ifosfamide, methotrexate (250–1000 mg/m²), mitoxantrone (≤ 15 mg/m²)	*Level 3 (30%–60% risk)* cyclophosphamide (≤ 750 mg/m²), oral cyclophosphamide, doxorubicin (20–69 mg/m²), epirubicin (≤ 90 mg/m²), hexamethylmelamine, idarubicin, ifosfamide, methotrexate (250–1,000 mg/m²), mitoxantrone (≤ 15 mg/m²)	
Moderately Low	*Intermediate (10%–30% risk)* *listed in order of decreasing risk:* irinotecan, mito-xantrone, paclitaxel, docetaxel, mitomycin C, topotecan, gemcitabine, etoposide, teniposide	*Level 2 (10%–30% risk)* asparaginase, cytarabine (< 1 gm/m²), docetaxel, doxorubicin (< 20 mg/m²), etoposide, fluorouracil (< 1,000 mg/m²), gemcitabine, methotrexate (51–249 mg/m²), mitomycin, paclitaxel, teniposide, thiotepa, topotecan	*Level 2 (10%–30% risk)* docetaxel, etoposide, fluorouracil (< 1,000 mg/m²), gemcitabine, methotrexate (51–249 mg/m²), mitomycin, paclitaxel	*Low-Moderate (10%–30% risk)* docetaxel, etoposide, fluorouracil (< 1,000 mg/m²), gemcitabine, methotrexate (51–249 mg/m²), mitomycin, paclitaxel
Low	*Low (< 10% risk)* *listed in order of decreasing risk:* vinorelbine, fluorouracil, methotrexate, thioguanine, mercaptopurine, L-asparaginase, vindesine, vinblastine, vincristine, busulfan, chlorambucil, melphalan, hydroxyurea, fludarabine, cladribine, tamoxifen	*Level 1 (< 10% risk)* androgens, bleomycin, busulfan, chlorambucil, cladribine, corticosteroids, fludarabine, hydroxyurea, interferon, melphalan, mercaptopurine, methotrexate (≤ 50 mg/m²), thioguanine, tretinoin, vinblastine, vincristine, vinorelbine	*Level 1 (< 10% risk)* Bleomycin, busulfan, chlorambucil, cladribine, fludarabine, hydroxyurea, melphalan, methotrexate (≤ 50 mg/m²), thioguanine, vinblastine, vincristine, vinorelbine	*Low (< 10% risk)* Bleomycin, busulfan, chlorambucil, cladribine, fludarabine, hydroxyurea, melphalan, methotrexate (≤ 50 mg/m²), thioguanine, vinblastine, vincristine, vinorelbine

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Guideline Development

All four guidelines were developed by panels consisting of experts in chemotherapy- and radiation therapy-induced N/V. The NCCN, ASHP, and ASCO expert panels are multidisciplinary, including medical and radiation oncology physicians, oncology nurses and oncology pharmacists. These expert panels reviewed the vast literature regarding antiemetics in cancer care and developed clinical practice guidelines based on both the strength of the evidence and the panel consensus. The guidelines employed slightly different criteria for evaluating the quality of the literature, with the ASHP and ASCO groups adhering most stringently to accepted standards for the development of evidence-based clinical practice guidelines. Nonetheless, there are more similarities than differences among these antiemetic guidelines. All of the guidelines make recommendations regarding the management of N/V due to chemotherapy or radiation therapy. The ASHP guidelines also address postoperative N/V, which will not be covered in this article.

Chemotherapy-Induced N/V

Classification of Emetogenicity

Although several factors can influence the risk of developing N/V following chemotherapy, the most powerful determinant is the emetogenic potential of the antineoplastic drugs used. Perhaps the most important difference among the four guidelines lies in classifying this emetogenic potential (Table 2). The NCCN guidelines use a 5-tier classification of N/V risk (i.e., levels 1–5 corresponding with a low, moderately low, moderate, moderately high, and high emetogenic potential). Previously published by Hesketh et al,[7] this 5-tier classification system includes recommendations for estimating the emetogenic potential of combination chemotherapy regimens. The MASCC guidelines employ a 4-tier classification system (ie, low, low-moderate, moderate-high, and high potential) almost identical to the NCCN system, except that levels 3 and 4 are collapsed into one category, "moderate-high." ASHP uses the 5-tier Hesketh system as a base, but updates the classification to include new anticancer agents. The ASCO expert panel creates a 3-tier classification (ie, low, intermediate, and high potential), but separates cisplatin into a subclass of its own within the high-risk category. Their system does not specify the role of dose in determining the level of emetogenic risk. For example, cyclophosphamide, cytarabine, and doxorubicin are classified as high risk, regardless of dose.

Although considerable overlap exists among the classification schemes used by the four groups, a few discrepancies about the emetic potential of certain chemotherapy agents exist. For example, irinotecan is classified as an agent of moderate to high emetogenic potential (30%–90% incidence) by MASCC, and as a level-4 agent (60%–90% incidence) by ASHP, but only as an intermediate-risk agent (10%–30% incidence) by ASCO. Mitoxantrone is classified as a level-3 agent (30%–60% incidence) by NCCN and ASHP and a moderate-high–risk agent by MASCC, but only an intermediate-risk agent by ASCO. Similarly, 5-fluorouracil is classified as a level 2 or intermediate-risk agent (10%–30% incidence) by MASCC, NCCN, and ASHP, but is only a low-risk agent (<10% incidence) according to ASCO. Monitoring outcomes resulting from the use of the antiemetic guidelines will clarify these discrepancies and influence the selection of antiemetics.

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Acute N/V

N/V occurring in the first 24 hours after chemotherapy is arbitrarily defined as acute N/V. For prevention of acute N/V due to cisplatin, the guidelines unanimously recommend the use of a 5-HT_3–receptor antagonist combined with a corticosteroid (Table 3). A wealth of evidence documents the superior efficacy of this combination compared with either older metoclopramide-based regimens or 5-HT_3–receptor antagonists alone. Approximately 75% of patients will likely achieve complete protection from N/V with this combination. In addition, the 5-HT_3–receptor antagonists are associated with fewer adverse effects than are older antiemetic regimens.

For other patients in whom an emetogenic agent is highly likely to cause N/V (30%–90% incidence), the combination of a 5-HT_3–receptor

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Table 3. *Guidelines for Prevention of Chemotherapy-Induced N/V in Adults**

Acute	*High risk, cisplatin* 5-HT_3–RA + steroid (I, A) *High risk, noncisplatin*, 5-HT_3–RA + steroid (I–III; A–B) *Intermediate risk*, steroid alone (III–IV; B,D) *Low risk* no antiemetics (V,D)	*Levels 3–5* 5-HT_3–RA + steroid (A) *Level 2* steroid alone (B) *Level 1* no antiemetics	*Levels 3–5* 5-HT_3–RA + steroid ± lorazepam (1-2) *Level 2* steroid or prochlorperazine or MCP + BEN (1) *Level 1* no antiemetics (1)	*High risk, cisplatin* 5-HT_3–RA + steroid (high) *Moderate-high risk, single-dose doxorubicin, epirubicin, carboplatin, or cyclophosphamide*, 5-HT_3–RA + steroid (high) *Low and repeated doses of cisplatin*, 5-HT_3–RA + steroid (high) *Oral CMF*, steroid + MCP (moderate) *Low-moderate risk*, no agreement on recommendation *Low risk*, no agreement on recommendation
Delayed	*Cisplatin* steroid + either MCP or 5-HT_3–RA (I, A) *Noncisplatin* steroid alone, steroid + MCP, or steroid + 5-HT_3–RA (III–IV, B–D)	*Cisplatin* steroid + either MCP or 5-HT_3–RA (A) *Cyclophosphamide, carboplatin, or doxorubicin* 5-HT_3–RA + steroid (B)	*Cisplatin* steroid alone, or + either MCP or 5-HT_3–RA (1) *Cyclophosphamide, carboplatin, or doxorubicin* steroid alone, or + either MCP or 5-HT_3–RA (2)	*Cisplatin* steroid + either MCP or 5-HT_3–RA (high) *Cyclophosphamide, carboplatin, epirubicin, or doxorubicin*, steroid alone or 5-HT_3–RA alone or steroid 5-HT_3–RA (moderate) *Low and repeated doses of cisplatin* 5-HT_3–RA + steroid (high)
Anticipatory	Prevent acute N/V (III, D), behavioral therapy or desensitization (III, B)	No recommendation	Prevent acute N/V, behavioral therapy, desensitization, or BZD (2)	Alprazolam (BZD) (moderate), desensitization, or hypnosis (high)

*Levels of evidence and/or confidence depicted in parentheses throughout the table are defined in Table 1.

BEN=diphenhydramine; BZD=benzodiazepine(s); 5-HT_3–RA =serotonin type-3–receptor antagonist; MCP=metoclopramide; oral CMF=oral cyclophosphamide, IV methotrexate, IV fluorouracil.

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antagonist and a corticosteroid is recommended by the NCCN, ASHP, and ASCO guidelines; 85% to 90% of patients are expected to achieve complete protection from N/V with this combination. The MASCC guideline is somewhat different because this recommendation does not apply to all agents within the moderate-high–risk category. The MASCC guidelines recommend a 5-HT_3–receptor antagonist in combination with a corticosteroid for regimens containing single IV doses of carboplatin, cyclophosphamide, doxorubicin, or epirubicin, and low and repeated doses of cisplatin (20–40 mg/m²/d for 3–5 days).

For prevention of acute N/V due to chemotherapy of intermediate or level-2 emetic risk (10%–30%), the NCCN, ASHP, and ASCO guidelines recommend use of a corticosteroid alone as initial therapy. Unfortunately, few published high-quality clinical trials have evaluated this class of emetogenic risk, and the level of evidence to support the recommendation in all the guidelines is poor, at best. Therefore, the MASCC has not made recommendations for this level of emetogenicity. Based on feedback from the NCCN members-at-large, the NCCN guidelines also include prochlorperazine, thiethylperazine, or metoclopramide plus diphenhydramine as acceptable choices for level 2 chemotherapy. Although this modification may best represent actual clinical practice, evidence supporting this recommendation is scarce. The guidelines are all consistent in recommending that no prophylactic antiemetics be given to patients receiving chemotherapy of the lowest emetogenic risk (<10%), although providing antiemetics for use on an as-needed basis was deemed acceptable for patients who experience symptoms. Again, however, evidence supporting this recommendation is weak because few clinical studies have addressed this class of agents.

Delayed N/V

This type of N/V begins 24 or more hours after chemotherapy administration and may last two to five days. The agent most notorious for this pattern of delayed emesis is cisplatin. The MASCC, ASHP, and ASCO guidelines strongly agree that the combination of dexamethasone with either metoclopramide or a 5-HT_3–receptor antagonist is associated with the lowest incidence of cisplatin-induced delayed N/V (30%) (Table 3). However, the NCCN guidelines also recommend the use of either a 5-HT_3–receptor antagonist or dexamethasone alone. All of the guidelines advocate dexamethasone alone or in combination with either 5-HT_3–receptor antagonists or metoclopramide for three to five days for other agents associated with delayed emesis, such as carboplatin, cyclophosphamide, doxorubicin, and epirubicin; however, the strength of evidence to support this recommendation varies widely.

5-HT_3–Receptor Antagonists

The antiemetic guidelines also address the selection of type, administration route, and dose of the 5-HT_3–receptor antagonists, including dolasetron, granisetron, or ondansetron (Table 4). The guidelines agree that all 5-HT_3–receptor antagonists produce equivalent results and are equally well tolerated. Basing product selection on convenience, availability, and cost, therefore, is reasonable. Orally administered 5-HT_3–receptor antagonists are as effective and more convenient to administer and cost-effective as their intravenous (IV) counterparts. Therefore, most of the guidelines advocate oral therapy whenever possible.

Although the four groups vary in their recommendations regarding the appropriate dose of

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5-HT_3–receptor antagonists, all of the guidelines conclude that parenteral ondansetron 8 mg produces results equivalent to those observed with higher ondansetron doses (i.e., 32 mg). Granisetron dose recommendations are either 10 mg/kg or 1 mg IV, whereas dolasetron recommendations are 1.8 mg/kg or 100 mg IV. There is less agreement regarding the doses of oral 5-HT_3–receptor antagonists, largely because fewer clinical trials have evaluated oral ondansetron and dolasetron with highly emetogenic chemotherapy, such as cisplatin. The MASCC guideline suggests a range of doses for oral ondansetron (12–16 mg bid or tid) and dolasetron (100–200 mg qd), which should be based on the emetogenic potential of the chemotherapy regimen (i.e., moderate vs high emetogenicity).

The guidelines vary in their approaches to special populations, including pediatric patients, patients receiving high-dose chemotherapy before bone marrow transplantation, and patients who fail their initial antiemetic regimen (Table 4).

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Table 4. *5-HT_3–Receptor Antagonist Selection Criteria**

Equivalency	All agents equally effective (I, A)	All agents equally effective(A)	All agents equally effective	All agents equally effective
Administration	Oral agents when possible; single doses when possible (I, A)	Oral agents when possible (B)	Oral agents when possible	Oral and IV
Dose	DOL 100 mg PO or 100 mg IV (1.8 mg/kg)	DOL 100–200 mg PO or 100 mg IV (1.8 mg/kg)	DOL 100 mg PO or 100 mg IV (1.8 mg/kg)	DOL 200 mg PO or 1.8 mg/kg IV
	GRAN 2 mg PO or 1 mg IV (10 mg/kg)	GRAN 2 mg PO or 10 mg/kg IV	GRAN 2 mg PO or 10 mg/kg IV	GRAN 2 mg PO or 10 mg/kg IV
	OND 12-24 mg PO or 8 mg IV (0.15 mg/kg)	OND 24 mg PO or 8 mg IV	OND 16 mg PO or 8 mg IV	OND 24 mg PO or 8 mg IV
Special populations				
Pediatrics	5-HT_3–RA + steroid for high risk; avoid DA (III, B))	Same as for adults; avoid DA (B-C)	Not addressed	5-HT_3–RA + steroid (moderate)
High-dose chemotherapy	5-HT_3–RA + steroid (II-III, C)	Not addressed	Not addressed	5-HT_3–RA + steroid (NP)
Failure of initial regimen	Identify cause; add BZD or add or change to DA (V, D)	Add agent with different mechanism, or maximize current regimen, or both (D)	Continue breakthrough medication on a schedule; consider changing chemotherapy regimen (I)	Add metopimazine (low)

*Levels of evidence and/or confidence depicted in parentheses throughout the table are defined in Table 1.

BZD=benzodiazepine(s); DA=dopamine receptor antagonist; DOL=dolasetron; GRAN=granisetron; NP=not possible; OND=ondansetron.

Radiation Therapy–Induced N/V

Few large, well-designed antiemetic trials have addressed the prevention of radiation therapy–induced N/V. As a result, the recommendations among the antiemetic guidelines are more varied. All of the guidelines classify total body irradiation and radiation therapy of the upper abdomen as high-risk factors for N/V development, and recommend a 5-HT_3–receptor antagonist for emesis prophylaxis. The MASCC and ASCO guidelines advocate adding a corticosteroid to the 5-HT3–receptor antagonist for high-risk patients. There is less agreement as to what type of radiation field constitutes a moderate risk of N/V, although both the MASCC and ASCO guidelines recommend a 5-HT_3–receptor antagonist alone in this situation. Neither the NCCN nor the ASHP guidelines recommend routine emesis prophylaxis for any type of radiation therapy other than total body or upper abdominal irradiation.

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Table 5. *Guideline for Prevention of RT-Induced N/V**

High risk Total body irradiation	5-HT_3–RA ± steroid (II–III, B-C)	5-HT_3–RA (B)	5-HT_3–RA (1)	5-HT_3–RA ± steroid (moderate–high)
Upper or whole abdomen	5-HT_3–RA or DA (II–III, B)	5-HT_3–RA (B)	5-HT_3–RA (1)	5-HT_3–RA ± steroid (moderate–high)
Intermediate risk Thorax, pelvis, lower hemithorax	5-HT_3–RA or DA (also includes mantle or craniospinal XRT or cranial radiosurgery) (II–III, B)	No recommendation	PRN antiemetics only	5-HT_3–RA (high)
Low risk	PRN antiemetics only (IV-V, B–D)	No recommendation	PRN antiemetics only	PRN antiemetics only

*Levels of evidence and/or confidence are depicted in parentheses throughout the table. See Table 1 for definitions of levels of evidence and/or confidence, ie, I-V, A-D, low, moderate, high.

BEN=diphenhydramine; BZD=benzodiazepine(s); DA=dopamine receptor antagonist; DOL=dolasetron; 5-HT_3–RA=serotonin type 3 receptor antagonist; GRAN=granisetron; OND=ondansetron; oral CMF=oral cyclophosphamide, IV methotrexate, IV fluorouracil; PRN=as needed; RT=radiation therapy.

Conclusions

The four clinical practice guidelines for use of antiemetics in oncology patients provide a balanced interpretation of the literature and set the standard of patient care. As these guidelines become more widely adopted into clinical practice, patient outcomes will need to be monitored, documented, and shared with colleagues. Through these efforts, the outcomes for future patients may be optimized.

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FDA Approves Mylotarg® for Acute Myeloid Leukemia

In May, 2000, gemtuzumab ozogomicin (Mylotarg®, Wyeth Ayerst Laboratories) was FDA-approved for the treatment of CD33-positive acute myeloid leukemia (AML) in patients over 60 years of age in first relapse or in whom chemotherapy is not a viable option. Mylotarg is a recombinant humanized antibody linked with a potent antitumor antibiotic, calicheamicin, isolated from a bacterium in a caliche clay soil sample from Texas. The antibody portion of Mylotarg binds specifically to the CD33 antigen, a glycoprotein commonly expressed by myeloid leukemic cells and other hematopoietic cells, but not on pluripotent stem cells.

In three multinational phase II trials involving 142 patients, Mylotarg produced a 26% overall response rate (ORR) in elderly (> 60 years) CD33-positive AML patients in first relapse. The median duration of overall survival was 5.9 months. The effectiveness of Mylotarg was based on ORRs; there are no controlled trials demonstrating a clinical benefit, such as improvement in disease-related symptoms or increased survival, compared with any other treatment.

Myelosuppression is the most common adverse event reported with Mylotarg; however, a postinfusion symptom complex of fever and chills, and, less commonly, hypotension and dyspnea during the first 24 hours after administration is also commonly observed. Some patients developed severe liver function abnormalities, which are generally transient and reversible. The most common adverse events include fever, chills, nausea, vomiting, thrombocytopenia, neutropenia, asthenia, diarrhea, abdominal pain, headache, stomatitis, dyspnea, epistaxis, and hypokalemia.

The manufacturer-recommended dosage of Mylotarg is 9 mg/m² administered as a 2-hour IV infusion in 2 doses given 14 days apart. Oral diphenhydramine (50 mg) and acetaminophen (650–1000 mg) should precede each dose. Acetaminophen may be repeated every 4 hours as needed thereafter.

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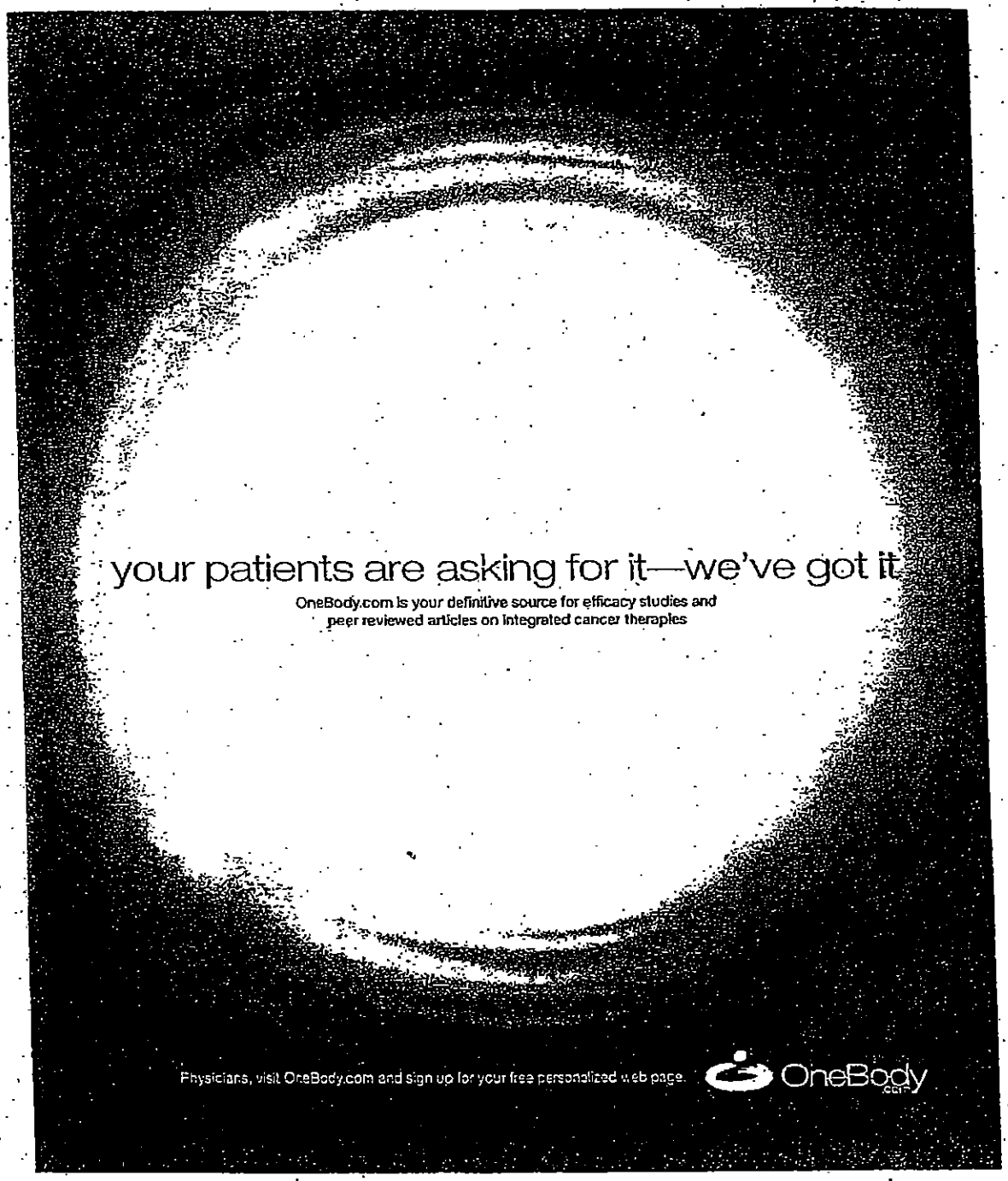

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Average Wholesale Prices and 2000 HCPCS Codes

The Average Wholesale Prices (AWPs) and HCPCS codes for drugs commonly used in cancer treatment are provided for your use as a reimbursement resource. Products are listed alphabetically by their generic name. The AWPs are obtained from the *2000 Red Book* and updates. For drugs that have multiple manufacturers, the AWP for the product most commonly stocked by OTN is listed. For ease of use, we list the AWP information in the first three columns and the billing code and units in the next two columns. Please refer to the *Sourcebook* for a complete listing of HCPCS codes.

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Proleukin®						
Aldesleukin	22 MIU	53905-0991-01	[illegible]	J9015	[illegible]	800-775-7533
Ethyol®						
Amifostine	500 mg	17314-7253-03	[illegible]	J0207	[illegible]	800-609-1083
Fungizone®						
Amphotericin B Oral Susp	25 ml	00087-1162-10	[illegible]	J0285	[illegible]	800-872-8718
Blenoxane®						
Bleomycin Sulfate, pwd	15 Units	00015-3010-20	[illegible]	J9040	[illegible]	800-872-8718
Bleomycin Sulfate, pwd	30 Units	00015-3063-01	[illegible]	J9040	[illegible]	800-872-8718
Xeloda®						
Capecitabine 150mg Tablet	120 Tabs	00004-1100-51	[illegible]	J8520	[illegible]	800-443-6676
Capecitabine 500mg Tablets	240 Tabs	00004-1101-76	[illegible]	J8521	[illegible]	800-443-6676
Paraplatin®						
Carboplatin, pwd	50 mg	00015-3213-30	[illegible]	J9045	[illegible]	800-872-8718
Carboplatin, pwd	150 mg	00015-3214-30	[illegible]	J9045	[illegible]	800-872-8718
Carboplatin, pwd	450 mg	00015-3215-30	[illegible]	J9045	[illegible]	800-872-8718

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PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
BiCNU®						
Carmustine, pwd	100 mg	00015-3012-38	[illegible]	J9050	100mg	800-872-8718
Platinol®-AQ						
Cisplatin 1mg/ml, inj	50 ml MDV	00015-3220-22	[illegible]	J9062	50mg	800-872-8718
Cisplatin 1mg/ml, inj	100 ml MDV	00015-3221-22	[illegible]	J9062	50mg	800-872-8718
Leustatin®						
Cladribine 1mg/ml, inj	10 mg	59676-0201-01	562.80	J9065	1mg	800-553-3851
Cytogam®						
Cytomegalovirus Immune Globulin	50 ml	60574-3101-01	690.81	J0850	Per vial	
Cytoxan® lyophilized						
Cyclophosphamide Lyopholized	100 mg	00015-0539-41	6.45	J9093	100mg	800-872-8718
Cyclophosphamide Lyopholized	200 mg	00015-0546-41	12.25	J9094	200mg	800-872-8718
Cyclophosphamide Lyopholized	500 mg	00015-0547-41	25.71	J9095	500mg	800-872-8718
Cyclophosphamide Lyopholized	1 Gram	00015-0548-41	51.43	J9096	1 Gram	800-872-8718
Cyclophosphamide Lyopholized	2 Gram	00015-0549-41	102.86	J9097	2 Gram	800-872-8718
Cytoxan® Tablets						
Cyclophosphamide 25mg Tablet	100 Tab	00015-0504-01	23.27	J8530	25mg	800-872-8718
Cyclophosphamide 50mg Tablet	100 Tab	00015-0503-01	41.85	J8530	25mg	800-872-8718
Cyclophosphamide 50mg Tablet	1000 Tab	00015-0503-02	418.50	J8530	25mg	800-872-8718
ARA-C®						
Cytarabine pwd	100 mg	55390-0131-10	6.00	J9100	100mg	
Cytarabine pwd	500 mg	55390-0132-10	30.00	J9110	500mg	
Cytarabine pwd	1 Gram	55390-0133-01	60.00	J9110	500mg	
Cytarabine pwd	2 Gram	55390-0134-01	120.00	J9110	500mg	
DTIC-Dome®						
Dacarbazine, pwd	200 mg	00026-8151-20	70.00	J9140	200mg	800-998-9180
DaunoXome®						
Daunorubicin citrate liposome 2mg/ml inj	25 ml	56146-0301-01	340.00	J9151	10mg	800-226-2056
Cerubidine®						
Daunorubicin HCl, pwd	20 mg	55390-0281-10	168.00	J9150	10mg	
DDAVP®						
Desmopressin Acetate 4mcg/ml	1 ml	00075-2451-01	24.20	J2597	1mcg	610-454-8110
Zinecard™						
Dexrazoxane, pwd	250 mg	00013-8215-62	118.00	J1190	250mg	800-808-9111
Dexrazoxane, pwd	500 mg	00013-8725-89	236.00	J1190	250mg	800-808-9111
Benadryl®						
Diphenhydramine HCl 50mg/ml inj	1 ml	00641-0376-25	0.41	J1200	50mg	
Taxotere®						
Docetaxel 20mg/0.5ml, inj	1 ml	00075-8001-20	45.51	J9170	20mg	800-996-6626
Docetaxel 20mg/0.5ml	1 ml	00075-8001-80	45.51	J9170	20mg	800-996-6626
Anzemet®						
Dolasetron 20mg/ml, inj	1 ml	00088-1206-32	12.00	J1260	100mg	800-221-4025
Rubex®						
Doxorubicin HCl, pwd	10 mg	00015-3352-22	7.00	J9000	10mg	800-872-8718
Doxorubicin HCl, pwd	50 mg	00015-3353-22	35.00	J9000	10mg	800-872-8718
Doxorubicin HCl, pwd	10 mg	55390-0231-10	7.00	J9000	10mg	
Doxorubicin HCl, pwd	50 mg	55390-0232-10	35.00	J9000	10mg	
Doxorubicin HCl, pwd	150 mg	55390-0233-01	105.00	J9000		
Doxorubicin HCl 2mg/ml, inj	5 ml	55390-0235-10	7.00	J9000		
Doxorubicin HCl 2mg/ml, inj	25 ml	55390-0236-10	35.00	J9000		
Doxorubicin HCl 2mg/ml, inj	100 ml	55390-0237-01	140.00	J9000		
Doxorubicin HCl 2mg/ml, inj	200 ml	55390-0238-01	280.00	J9000		
Adriamycin™						
Doxorubicin RDF, pwd	10 mg	00013-1086-91	7.00	J9000		800-242-7014
Doxorubicin RDF, pwd	50 mg	00013-1106-79	35.00	J9000		800-242-7014
Doxorubicin RDF, pwd	150 mg	00013-1116-83	105.00	J9000		800-242-7014
Doxorubicin HCl pfs 2mg/ml, inj	5 ml	00013-1136-91	7.00	J9000		800-242-7014
Doxorubicin HCl pfs 2mg/ml	25 ml	00013-1146-91	35.00	J9000		800-242-7014
Doxorubicin HCl pfs 2mg/ml	100 ml	00013-1156-79	140.00	J9000		800-242-7014
Doxorubicin HCl pfs 2mg/ml	200 ml	00013-1176-87	280.00	J9000		800-242-7014
Doxorubicin HCl pfs 2mg/ml	250 ml	00013-1166-83	350.00	J9000		800-242-7014
Doxil®						
Doxorubicin, HCL liposome 2mg/ml inj	10 ml	61471-0295-12	250.00	J9001	10mg	800-609-1082

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Procrit®						
Epoetin Alpha 2000u/ml inj	1 ml	59676-0302-01	25.00	Q0136	1,000units	800-553-3851
Epoetin Alpha 3000u/ml inj	1 ml	59676-0303-01	37.40	Q0136	1,000units	800-553-3851
Epoetin Alpha,4000u/ml inj	1 ml	59676-0304-01	49.87	Q0136	1,000units	800-553-3851
Epoetin Alpha 10, 000u/ml inj	1 ml	59676-0310-01	124.68	Q0136	1,000units	800-553-3851
Epoetin Alpha 20, 000u/ml inj	1 ml	59676-0320-01	249.36	Q0136	1,000units	800-553-3851
Epoetin Alpha 40, 000u/ml inj	1 ml	59676-0340-01	498.72	Q0136	1,000units	800-553-3851
VePesid®						
Etoposide 50mg Capsule	20 caps	00015-3091-45	1,020.54	J8560	50mg	800-872-8718
Etoposide 20mg/ml, inj	5 ml	00015-3095-20	136.49	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	7.5 ml	00015-3084-20	204.74	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	25 ml	00015-3061-20	665.38	J9182	100mg	800-872-8718
Etoposide 20mg/ml, inj	50 ml	00015-3062-20	1,296.64	J9182	100mg	800-872-8718
Etopophos®						
Etoposide Phosphate, pwd	100 mg	00015-3404-20	124.14		100mg	800-872-8718
Fludara®						
Fludarabine Phosphate, pwd	50 mg	50419-0511-06	259.50	J9185	50mg	800-473-5832
5FU®						
Fluorouracil 50mg/ml, inj	10 ml	00013-1036-91	3.20	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	50 ml	00013-1046-94	16.04	J9190	500mg	800-242-7014
Fluorouracil 50mg/ml, inj	100 ml	00013-1056-94	32.06	J9190	500mg	800-242-7014
Neupogen®						
Filgrastim(G-CSF) 300mcg/ml, inj	300 mcg	55513-0530-10	180.40	J1440	300mcg	800-272-9376
Filgrastim(G-CSF) 300mcg/ml, inj	480 mcg	55513-0546-10	274.40	J1441	480mcg	800-272-9376
Gemzar®						
Gemcitabine HCL pwd	200 mg	00002-7501-01	99.12	J9201	200mg	888-443-6927
Gemcitabine HCL pwd	1 Gram	00002-7502-01	497.72	J9201	200mg	888-443-6937
Leukine®						
Sargramostim(GM-CSF), pwd	250 mcg	58406-0002-33	144.30	J2820	50mcg	800-321-4669
Sargramostim(GM-CSF) 500mcg/ml, inj	1 ml	58406-0050-30	288.59	J2820	50mcg	800-321-4669
Zoladex®						
Goserelin Acetate, implant	3.6 mg syringe	00310-0960-36	469.99	J9202	3.6mg	800-400-4140
Goserelin Acetate, implant	10.8 mg syringe	00310-0961-30	1,409.98	J9202	3.6mg	800-400-4140
Kytril®						
Granisetron HCl 1mg/ml, inj	1 ml	00029-4149-01	195.20	J1626	100mcg	800-699-3806
Granisetron HCl 1mg/ml, inj	4 ml	00029-4152-01	780.80	J1626	100mcg	800-699-3806
Ifex®						
Ifosfamide pwd	1 Gram	00015-0556-41	157.04	J9208	1gm	800-872-8718
Ifosfamide pwd	3 Gram	00015-0557-41	471.11	J9208	1gm	800-872-8718
Ifex®/Mesnex™						
Ifosfamide(10x1g)/Mesna(10x1g MDV)	Combo-Pack	00015-3554-27	2,610.16	J9208/J9209	1gm/200mg	800-872-8718
Ifosfamide(2x3g)/Mesna(6x1g MDV)	Combo-Pack	00015-3564-15	1,566.03	J9208/J9209	1gm/200mg	800-872-8718
Ifosfamide(5x1g)/Mesna(3x1g MDV)	Combo-Pack	00015-3556-26	1,080.21	J9208/J9209	1gm/200mg	800-872-8718
Venoglobulin S						
Immune Globulin 50mg/ml, inj w/IV set	50 ml	49669-1612-01	225.00	J1561	500mg	
Immune Globulin 50mg/ml, inj w/IV set	100 ml	49669-1613-01	450.00	J1561	500mg	
Immune Globulin 50mg/ml, inj w/IV set	200 ml	49669-1614-01	900.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	50 ml	49669-1622-01	475.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	100 ml	49669-1623-01	950.00	J1561	500mg	
Immune Globulin 100mg/ml, inj w/IV set	200 ml	49669-1624-01	1,900.00	J1561	500mg	
Immune Globulin 100mg/ml, inj	10 ml	00026-0648-12	90.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	50 ml	00026-0648-20	450.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	100 ml	00026-0648-71	900.00	J1561	500mg	800-998-9180
Immune Globulin 100mg/ml, inj	200 ml	00026-0648-24	1,800.00	J1561	500mg	800-998-9180
Immune Globulin, pwd	2.5 Gram	52769-0471-72	223.75	J1562	5Grams	
Immune Globulin, pwd	5 Gram	52769-0471-75	447.50	J1562	5Grams	
Immune Globulin, pwd	10 Gram	52769-0471-80	895.00	J1562	5Grams	
RHO (d) Immune Globulin, pwd	600 IU	60492-0021-01	142.00	J2792	100 IU	
RHO (d) Immune Globulin, pwd	1500 IU	60492-0023-01	324.50	J2792	100 IU	
RHO (d) Immune Globulin, pwd	5000 IU	60492-0024-01	1,081.50	J2792	100 IU	

OTN
ONCOLOGY THERAPEUTICS NETWORK

REIMBURSEMENT

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Intron®-A						
Interferon Alpha 2B 3MIU/0.5ml	3 MIU/0.5	00085-1184-02		J9214	3 MIU	800-521-7157
Interferon Alpha 2B 5MIU/0.5ml	5 MIU/0.5	00085-1191-02		J9214	5 MIU	800-521-7157
Interferon Alpha 2B 10MIU/ML	10MIU/1ML	00085-1179-02		J9214	10 MIU	800-521-7157
Interferon Alpha 2B 6MIU/ml, inj	18 MIU/3ml	00085-1168-01		J9214	18 MIU	800-521-7157
Interferon Alpha 2B, 10MIU/ML, inj	25 MIU	00085-1133-01		J9214	25 MIU	800-521-7157
Interferon Alpha 2B, pwd	3 MIU	00085-0120-02		J9214	3 MIU	800-521-7157
Interferon Alpha 2B, pwd	10 MIU	00085-0571-02		J9214	10 MIU	800-521-7157
Interferon Alpha 2B, pwd	18 MIU	00085-1110-01		J9214	18 MIU	800-521-7157
Interferon Alpha 2B, pwd	25 MIU	00085-0285-02		J9214	25 MIU	800-521-7157
Interferon Alpha 2B, pwd	50 MIU	00085-0539-01		J9214	50 MIU	800-521-7157
Roferon® A						
Interferon Alpha 2A 3MIU/ML, inj	3 MIU	00004-2009-09		J9213	3 MIU	800-443-6676
Interferon Alpha 2A 6MIU/ml, inj	6 MIU	00004-2007-09		J9213	6 MIU	800-443-6676
Interferon Alpha 2A 9MIU/0.9ml, inj	9 MIU	00004-2010-09		J9213	9 MIU	800-443-6676
Interferon Alpha 2A 6MIU/ml, inj	6 MIU	00004-2011-09		J9213	6 MIU	800-443-6676
Interferon Alpha 2A 36MIU/ml, inj	36 MIU	00004-2012-09		J9213	36 MIU	800-443-6676
Camptosar®						
Irinotecan HCL 20mg/ml, inj	2ml	00009-7529-02		J9206	100 mg	800-242-7014
Irinotecan HCL 20mg/ml, inj	5ml	00009-7529-01		J9206	250 mg	800-242-7014
Leucovorin®						
Leucovorin Calcium, pwd	50mg	55390-0051-10		J0640		
Leucovorin Calcium, pwd	100mg	55390-0052-10		J0640		
Leucovorin Calcium, pwd	350mg	55390-0053-01		J0640		
Leucovorin Calcium, pwd	350mg	58406-0623-07		J0640		800-321-4669
Lupron®						
Leuprolide Acetate, pwd	3.75mg	00300-3642-01		J9217		800-453-8438
Leuprolide Acetate, pwd	7.5mg	00300-3346-01		J9217		800-453-8438
Ativan®						
Lorazepam 2mg/ml, inj	1ml	00008-0581-04		J2060		
Lorazepam 2mg/ml, inj	10ml	00008-0581-01		J2060		
Lorazepam 4mg/ml, inj	1ml	00008-0570-01		J2060		
Lorazepam 2mg/ml, inj	1ml	00008-0581-02		J2060		
Mannitol®						
Mannitol 25%, inj	50ml	00074-4031-01		J2150		
Mustargen®						
Mechlorethamine HCL pwd	10mg	00006-7753-31		J9230		800-994-2111
Megace®						
Megestrol Acetate 20mg Tablet	100	00015-0595-01				800-872-8718
Megestrol Acetate 40mg Tablet	100	00015-0596-41				800-872-8718
Megestrol Acetate 40mg Tablet	240	00015-0596-46				800-872-8718
Megestrol Acetate 40mg Tablet	1000	00015-0596-45				800-872-8718
Megestrol Acetate oral susp 40mg/ml	240ml	00015-0508-42				800-872-8718
Alkeran®						
Melphalan HCL, pwd	50mg	00173-0130-93		J9245		800-722-9294
Melphalan 2mg Tablet	25	00173-0045-35		J8600		800-722-9294
Mesnex™						
Mesna 100mg/ml, inj	10ml	00015-3563-02		J9209		800-872-8718
Methotrexate®						
Methotrexate Sodium, pwd	50mg	58406-0673-01		J9250		800-321-4669
Methotrexate Sodium, pwd	100mg	58406-0671-05		J9260		800-321-4669
Methotrexate Sodium 25mg/ml, inj	2ml	55390-0031-10		J9260		
Methotrexate Sodium 25mg/ml, inj	10ml	55390-0032-10		J9260		
Methotrexate Sodium 25mg/ml, inj	20ml	55390-0033-10		J9260		
Methotrexate Sodium 25mg/ml, inj	40ml	55390-0034-10		J9260		
Methotrexate Sodium 25mg/ml, inj	2ml	58406-0681-14		J9260		800-321-4669
Methotrexate Sodium 25mg/ml, inj	10ml	58406-0681-17		J9260		800-321-4669
Methotrexate Sodium 2.5mg Tablet	100	00555-0572-02		J8610		
Methotrexate Sodium 2.5mg Tablet	500	00555-0572-35		J8610		
Mutamycin®						
Mitomycin, pwd	5mg	00015-3001-20		J9280		800-872-8718
Mitomycin, pwd	20mg	00015-3002-20		J9290		800-872-8718
Mitomycin, pwd	40mg	00015-3059-20		J9291		800-872-8718

REIMBURSEMENT

ONCOLOGY THERAPEUTICS NETWORK

PRODUCT	VIAL SIZE	NDC#	AWP/VIAL	2000 HCPCS	BILLING UNITS	HOTLINE NO.
Novantrone®						
Mitoxantrone HCl 2mg/ml, inj	10 ml	58406-0640-03	939.06	J9293	5mg	800-321-4669
Mitoxantrone HCl 2mg/ml, inj	12.5 ml	58406-0640-05	1,173.76	J9293	5mg	800-321-4669
Mitoxantrone HCl 2mg/ml, inj	15 ml	58406-0640-07	1,408.55	J9293	5mg	800-321-4669
Sandostatin®						
Octreotide Acetate 50mcg/ml, Inj	1 ml	00078-0180-03	6.61	J9999/J3490		800-257-3273
Octreotide Acetate 100mcg/ml, Inj	1 ml	00078-0181-03	12.83	J9999/J3490		800-257-3273
Octreotide Acetate 500mcg/ml, inj	1 ml	00078-0182-03	61.55	J9999/J3490		800-257-3273
Sandostatin LAR® Depot						
Octreotide Acetate, pwd	10 mg	00078-0340-84	1,422.13	J2352	1mg	800-257-3273
Octreotide Acetate, pwd	20 mg	00078-0341-8	1,422.13	J2352	1mg	800-257-3273
Octreotide Acetate, pwd	30 mg	00078-0342-84	2,133.19	J2352	1mg	800-257-3273
Zofran®						
Ondansetron HCL 2mg/ml, inj	20 ml	00173-0442-00	256.04	J2405	1mg	800-745-2967
Ondansetron HCL 2mg/ml, inj	2 ml	00173-0442-02	25.60	J2405	1mg	800-745-2967
Ondansetron 32mg/50ml, premixed bag	50 ml	00173-0461-00	206.41	J2405	1mg	800-745-2967
Neumega®						
Oprelvekin, pwd	5 mg	58394-0004-01	2487.75	J2355	5mg	888-638-6342
Taxol®						
Paclitaxel 6mg/ml, inj	30 mg	00015-3475-30	302.69	J9265	1mg	800-872-8718
Paclitaxel 6mg/ml, inj	100 mg	00015-3476-30	808.26	J9265	1mg	800-872-8718
Paclitaxel 6mg/ml, inj	300 mg	00015-3479-11	2426.29	J9265	1mg	800-872-8718
Aredia®						
Pamidronate disodium pwd	30 mg	00083-2601-04	166.44	J2430		800-257-3273
Pamidronate disodium pwd	90 mg	00083-2609-01	498.68	J2430		800-257-3273
Nipent™						
Pentostatin pwd	10 mg	62701-0800-01	1,245.00	J9268	10mg	800-340-8667
Compazine®						
Prochlorperazine 5mg/ml, inj	10 ml	00007-3343-01	47.00	J0780	10mg	800-699-3806
Prochlorperazine 10mg tab	100 tabs	00007-3367-20	299.50	Q0165	10mg	800-699-3806
Zantac®						
Ranitidine 25mg/ml, inj	2 ml	00173-0362-38	3.43	J2780		
Respigam®						
Respiratory Syncytial Virus Immune globul	20 ml	60574-2102-01	2,400.00	J1565		
Respiratory Syncytial Virus Immune globul	50 ml	60574-2101-01	5,250.00	J1565		
Rituxan™						
Rituximab 10mg/ml, inj	10 ml	50242-0051-21	345.00	J9310	100mg	800-530-3083
Rituximab 10mg/ml, Inj	50 ml	50242-0053-06	1,725.00	J9310	100mg	800-530-3083
Zanosar®						
Streptozocin, pwd	1 Gram	00009-0844-01	114.00	J9320		800-242-7014
Vumon®						
Teniposide 10mg/ml, Inj	5 ml	00015-3075-19	1,210.00	J9999	50mg	800-872-8718
Thioplex®						
Thiotepa, pwd	15 mg	58406-0661-02	13.25	J9340		800-321-4669
Hycamtin™						
Topotecan, pwd	4 mg	00007-4201-01	299.25	J9350		800-699-3806
Topotecan, pwd	10 mg	00007-4201-05	748.13	J9350		800-699-3806
Herceptin®						
Trastuzumab, pwd	440 mg	50242-0134-60	2,200.00	J9355		800-530-3083
Neutrexin®						
Trimetrexate, pwd	200 mg	58178-0020-10	1,000.00	J3305		800-887-2467
Trimetrexate, pwd	1000 mg	58178-0020-50	5,000.00	J3305		800-887-2467
Trimetrexate, pwd	250 mg	58178-0021-01	1,250.00	J3305		800-887-2467
Urokinase®						
Urokinase, pwd	250,000 IU	00074-6131-01	1,000.00	J3364		
Urokinase, pwd	5000 IU	00074-6145-02	20.00	J3364		
Velban®						
Vinblastine sulfate pwd	10 mg	55390-0091-10	27.00	J9360		
Vinblastine sulfate 1mg/ml, inj	10 ml	63323-0278-10	27.00	J9360		
Vincristine®						
Vincristine sulfate 1mg/ml, inj	1 ml	00013-7456-86	5.00	J9370		800-242-7014
Vincristine sulfate 1mg/ml, inj	1 ml	61703-0309-06	5.00	J9370		
Vincristine sulfate 1mg/ml, inj	2 ml	00013-7466-86	10.00	J9375		800-242-7014
Vincristine sulfate 1mg/ml, inj	2 ml	61703-0309-16	10.00	J9375		
Navelbine®						
Vinorelbine 10mg/ml, Inj	1 ml	00173-0656-01	79.48	J9390		800-423-6869
Vinorelbine 10mg/ml, Inj	5 ml	00173-0656-44	397.40	J9390		800-423-6869

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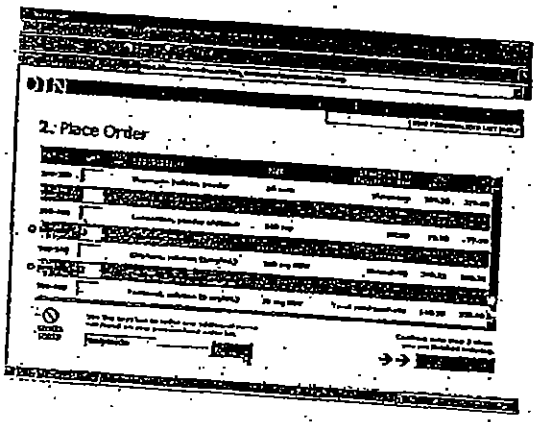

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Comments and suggestions are welcome. Address them to: Peggy Lehmann, Editor, The Network News Oncology Therapeutics Network 395 Oyster Point Blvd., Suite 405 So. San Francisco, CA 94080.

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